EXHIBIT I

FILED UNDER SEAL

In the Matter of:

FTC, et al. v. Quincy Bioscience Holding, et al.

September 29, 2021
Mindy Kurzer, Ph.D. - Confidential

Condensed Transcript with Word Index

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IN THE UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK

FEDERAL TRADE COMMISSION and THE PEOPLE OF THE STATE OF NEW YORK, by LETITIA JAMES, Attorney General of the State of New York,
Plaintiffs,
vs.
QUINCY BIOSCIENCE HOLDING COMPANY, INC., a corporation, et al,
Defendants.

CASE NO. 1:17-CV-00124-LLS

CONFIDENTIAL - ATTORNEYS' EYES ONLY

VIDEOTAPED DEPOSITION of MINDY KURZER, Ph.D. taken by Plaintiffs, held remotely, commencing at 8:32 A.M., on September 29, 2021, before Gary Schneider, RPR, CRR, RMR, TLCR and Notary Public within and for the State of Tennessee.

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I N D E X

WITNESS: MINDY KURZER

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REPORTER'S NOTES:
QUOTATION MARKS ARE USED FOR CLARITY AND DO NOT NECESSARILY REFLECT A DIRECT QUOTE

PROPER NAMES ARE PHONETICALLY SPELLED UNLESS STATED ON THE RECORD

P R O C E E D I N G S

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STIPULATION:
All counsel present stipulate that the witness shall be sworn remotely by the court reporter

* * *

THE VIDEOGRAPHER: Here begins disk 1 in the video deposition of Mindy Kurzer, Ph.D., taken in the matter of Federal Trade Commission and the People of the State of New York by Letitia James, Attorney General of the State of New York v. Quincy Bioscience Holding Company, et al., in the United States District Court, Southern District of New York, matter number 1:17-cv-00124-LLS.

Today's date is September 29th, 2021. The time on the video monitor is 8:32 A.M. Central. This deposition is being held remotely via Zoom video teleconference.

The court reporter is Gary Schneider on behalf of For The Record, Inc. The video camera operator is Eric Vavrasek on behalf of For The Record, Inc.

Will counsel please introduce themselves and state whom they represent beginning with the party noticing the deposition.

MR. WONE: Good morning. My name is Andrew Wone, and I'm appearing on behalf of the Federal Trade Commission. Also appearing on behalf of the Federal Trade Commission are attorneys Edward Glennon and Annette Soberats. And Investigator William Ducklow is also present.

MS. MATUSCHAK: This is Kate Matuschak, and I'm here for the New York State Attorney General's Office.

MS. METZINGER: This is Jaclyn Metzinger from Kelley Drye & Warren, LLC, on behalf of Quincy Bioscience Holding Company, Quincy Bioscience Science, LLC, Prevagen, Inc., and Quincy Bioscience Manufacturing, LLC. Also -- and for Dr. Kurzer as well.

Also with me today from Kelley Drye are Geoffrey Castello, Glenn Graham, and Caitlin Hickey.

MR. de LEEUW: Michael de Leeuw from Cozen O'Connor on behalf of Mark Underwood.

THE VIDEOGRAPHER: Will the court reporter please swear in the witness.

Whereupon --

MINDY KURZER, Ph.D.,

was called as a witness and, after having been first duly sworn, testified as follows:

E X A M I N A T I O N

BY MR. WONE:

Q. Good morning, Doctor.

A. Good morning.

Q. How do you pronounce your last name?

A. Kurzer.

Q. Kurzer.

A. I'm sorry, Mr. Wone. You were -- you were a little bit -- your audio wasn't following your video for a moment.

Q. Okay. Can you hear me fine now?

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A. I can hear you fine now.
Q. Great.
So I'll start off this morning thanking you for joining us today. I want to go over a few procedures which hopefully will make things a little bit easier for both of us today. Okay?
A. Yes.
Q. Today I'll be asking you a series of questions. If you don't hear a question, please say so and I'll repeat it. If you don't understand a question, please say so and I will try to rephrase it.
If you realize an answer that you gave earlier was inaccurate or incomplete, please let me know and you'll have -- you want to correct it or supplement it and -- you'll have a chance to do so.
If you'd like to take a break at any point, please let me know and we can accommodate you. My only request is if a question is pending, that you answer the question before we take a break.
Do you understand?
A. I do, yes.

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Q. If you answer a question, I'll assume you've heard it, understood it, and given me your best recollection.
Because the court reporter is -- because the deposition is being taken remotely, it's important that you answer all questions verbally. The court reporter cannot record hand gestures or nodding or shaking of heads.
Do you understand?
A. I do, yes.
Q. It's also important that only one person speak at a time, so if you could please let me finish my question before you begin your answer, and I will make sure to let you finish your answer before I ask my next question.
Today you should testify from your memory and from using the exhibits that were introduced.
Were you able to access AgileLaw?
A. Yes.
Q. Okay. So that program -- as we discussed last week in the trial run, that program will display all of the documents that you should use during today's deposition. I ask that you not

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consult other sources of information, so any papers, notes, cellphones, computers, tablets or any other device or document during the deposition.
Do you understand?
A. I do understand, yes.
Q. During the deposition, when we're on the record, you cannot communicate with anyone else, including your attorneys.
Do you understand?
A. Yes.
Q. The only exception to that is during breaks. During breaks, you're free to talk with your attorneys.
During the deposition, I will be showing you documents through AgileLaw. You'll have a chance to look at them, and then I will ask you some questions. The documents will be marked, like you saw last week in the lower right-hand corner of the first page, with an exhibit number. And during the course of the deposition, we'll be referring to those exhibit numbers for what document you should be looking at at a particular moment.
Do you understand the

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instructions?
A. I do understand the instructions, yes.
Q. And is there --
MS. METZINGER: And --
MR. WONE: -- any reason --
MS. METZINGER: Sorry. Go ahead.
MR. WONE: No, go on.
MS. METZINGER: I was just going to ask that, as we've done in prior depositions, designate the transcript, at least provisionally, as attorneys' eyes only pursuant to the protective order, and we will follow-up with more specific designations once we receive the transcript.
MR. WONE: Okay.
MS. METZINGER: Thank you.
BY MR. WONE:
Q. Dr. Kurzer, do you understand the instructions I gave you?
A. I do understand the instructions, yes.
Q. And can you think of any reason

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why you wouldn't be able to answer my questions today truthfully and fully?
A. No, there is no reason.
Q. Can you please state and spell your name for the record.
A. My name is Mindy Kurzer, M-I-N-D-Y, last name K-U-R-Z-E-R.
Q. Okay. I've introduced and marked the first Exhibit as MK1.
(Marked Exhibit MK1.)
BY MR. WONE:
Q. You should see that on your screen, Dr. Kurzer.
A. I do.
Q. Is Exhibit MK1 the expert report that you prepared for -- on behalf of the defendants in this case?
A. Yes, it is.
Q. And if you could turn to Exhibit A of your expert report or what's been designated as MK1, please.
A. And would that be at the very end or where -- where would that -- where would the exhibit be?
Q. It should start on approximately

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page 50, 50 out of 65.
A. Okay. Yes.
Q. And what is Exhibit A, Dr. Kurzer?
A. Exhibit A is my curriculum vitae.
Q. Where did you get your undergraduate degree, Mr. Kurzer?
A. My undergraduate degree was from the State University of New York at Buffalo.
Q. And what did you study at Buffalo?
A. I studied history and philosophy.
Q. And when did you graduate?
A. I graduated in 1973.
Q. And what did you do after you graduated?
A. After I graduated, I did some various kinds of work, and then I started a master's program at the University of California at Berkeley, master's in nutrition.
Q. And what was the nature of your work between graduating Buffalo and starting your master's program?

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A. I was a mail handler at the Post Office, and that was the primary work. I also was a substitute teacher in daycare centers.
Q. Can you describe your graduate program?
A. My graduate program was in nutritional science. I have a master's degree in nutritional science from the University of California Berkeley, and I also have a Ph.D. in nutritional science from the University of California at Berkeley. And nutritional science is a combination of physiology and biochemistry. It's a science-based degree, and I would say that it is an applied science. So it's the -- and I focused on human nutrition in my research. So I -- for my -- both my master's and my doctorate, I performed research and I published papers from that research, and they were primarily human clinical studies.
Q. Can you describe the topics or areas that your research focused on?
A. Sure.
So my doctoral project was a clinical study investigating the effect of a low-calorie diet on reproductive hormones in young

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women.
Q. Did you conduct that study yourself?
A. I was the -- as a student, I was not the principal investigator. My major advisor was the principal investigator for purposes of reporting and regulation, et cetera. I did -- I was the person who ran the study. I recruited the participants. I worked with them on the -- on a daily basis on all of the aspects of the study. And I also analyzed the data and wrote reports for publication.
Q. Was that study a randomized controlled trial?
A. It was not, no.
Q. What kind of study was it?
A. It was a -- it was a study in which each person was their own control. So rather -- a randomized control trial will have two separate groups, like parallel arm study, and this was -- this was not. So each person -- and it was a small study. They there were only six people. And the reason is because the University of California at Berkeley had a metabolic unit in which many of the studies that have been used to

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define requirements for nutrients such as protein were done on very small populations. It's a live-in unit where six people -- there were six beds. And metabolic -- this was a metabolic study and -- in which you study a small amount of people and you study them very intensively. And my study was designed to be performed in that metabolic unit. And, unfortunately, the metabolic unit grant was not renewed, and so my study was done on an outpatient basis. And -- and as a result, it was -- you know, we had to shift gears and pivot to do it on an outpatient basis. But it was a very small number of people. It was six woman, and they consumed either a regular diet, and I followed them for about six weeks, or I put them on a very low-calorie diet, about 40 percent of their required calories, for six weeks. And I measured reproductive hormones every other day because I was interested in the effect on the menstrual cycle, how energy deprivation and a low-calorie diet affects the menstrual cycle and reproductive hormones in young women. And so we measured hormones every other day on these women. Even though it was an outpatient study, they came into the -- to the facility, to the clinical

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facility.

Q. Were you involved in the design of the study?

A. I was, yes.

Q. Were you involved in any other research during your master's or Ph.D. programs at Berkeley?

A. Yes. I did some -- I participated and actually ran a few clinical trials because I had a gap of a couple of years between my master's and my Ph.D. during which I worked as a research scientist in the department and I ran a couple of different clinical trials, one of which was to evaluate the effect of consumption of beans, legumes, on gas production. And so we had a group of men who consumed a meal of beans and we collected their intestinal gas and measured it in order to -- and we gave them different fractions, different processed parts of the beans in order to determine what part -- portion of the beans was responsible for producing the gas. So that was one study that we did.

Another study was a study in which we had participants in the metabolic ward consuming exactly the same diet that they had

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consumed on the outside for a period of about two months. These participants lived in the metabolic ward for two or three months and they consumed a liquid diet. And in this case, in this -- generally. But in this study, they consumed the same diet that they had consumed on the outside. And the purpose was to try to validate the results of the real-life study with a controlled study in a controlled environment. And that was not a study that I designed. That was a study that I supervised, ran, recruited participants for, worked with the participants as an employee.

Q. When you say "running clinical trials," did it involve analyzing data?

A. For my own research, for the research that was part of my master's and my Ph.D., yes, it involved analyzing data. For the research which I -- in which I was acting as a staff member, I was not involved in analyzing the data. I was involved in running the trial, basically.

Q. Okay. Were you involved in running any other trials?

A. At that point, no. Those -- those were the studies that I was involved and

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highly responsible for as a student.

Q. Okay. Did any of your research work or coursework involve cognitive function?

A. No, only my own.

Q. And what was that? Oh, only your own.

A. Yes.

Q. Meaning yourself.

A. Yes. Sorry.

Q. I understand.

Okay. So what did you do after you finished your Ph.D. at Berkeley?

A. After I finished my Ph.D. at Berkeley, I was a postdoctoral fellow in San Francisco at the University of California San Francisco where I did very basic science work on endocrinology. I was very interested in the relationship between diet, nutrition, and hormones. And so I worked with a very well-known -- particularly reproductive hormones. So I worked with a very well-known scientist in the field of estrogen metabolism at the University of California San Francisco, and I did self-culture studies looking at the effects of various compounds on estrogen synthesis primarily

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in adipose cells.
Q. You used the phrase "basic science." What did you mean?
A. By this I mean I did not have human subjects. This was wet lab cell culture work, in vitro, in vitro work as opposed to human studies.
Q. Did any of your postgraduate work involve any aspect of cognitive functions?
A. No, it did not.
Q. What did you do after you finished this postgraduate work?
A. After I finished that postgraduate work, I actually -- I'm sorry, I'm getting two things chronologically mixed up. Directly after my -- my Ph.D., before I went to San Francisco, I received a NATO postdoctoral fellowship to work in Europe for a year to do research. And so for a year, in between Berkeley and San Francisco, I lived in Rome, and then I lived in Denmark performing nutrition research with -- with scientists there as a continuation of my training. So that was my first postdoc. And then the second postdoc was in San Francisco.
Q. What was the -- what was the

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focus of the first postdoc in Europe?
A. I did two different things. In Rome -- I was in Rome for four months and I worked at the National Institute of Nutrition in Rome with the director, and I helped them with some epidemiological studies of children, looking at reproductive hormones and diet at different ages in children. And so that was kind of a little bit of a training experience for me to just get to see what they were doing.
From there, I went to Odense, Denmark, to the University of Odense, and I worked in a lab with Loris Garbi, who was an expert in energy expenditure and energy metabolism, and I spent almost a year with him working on studies looking at energy expenditure and the factors that influence it in young people.
Q. Did any of your research in Europe involve randomized controlled trials?
A. No.
Q. Did any of your research in Europe -- while in Europe involve cognitive function?
A. No.
Q. So after you finished that

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postdoctorate work experience in Europe, then you went to San Francisco?
A. That's right, exactly. I came home, and then I started at San Francisco, and I was there for two and a half years.
Q. Okay. And what did you do after those two and a half years in San Francisco?
A. After the two and a half years in San Francisco, I took a position at the University of Minnesota as an assistant professor, and I've been there for over 30 years.
Q. Can you describe your work at the University of Minnesota?
A. Yes. At the University of Minnesota, I have a few different major responsibilities. One is research program, and my research program over the 30 years has focused -- it's shifted somewhat, but most of the 30 years has focused on human clinical studies, evaluating the effects of dietary substances and dietary supplements on health endpoints in humans and -- with particular interest in cancer prevention and heart health, et cetera, looking at biomarkers of these -- of these disease states. So not looking at the diseases themselves, but looking at markers

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of them. So that's been a lot of what I've done for my research.
I've had a pretty big research program. It has been primarily funded by the National Institutes of Health and other federal agencies, the Department of Defense, and very -- I have a little bit of corporate sponsorship of -- of some of my research, but very little. It's mainly federal sources. So that's been my research program.
I also teach. I teach nutrition. I've taught a few different courses. The main -- my main responsibility has been Introductory Nutrition which I teach to freshmen through senior primarily at the university. And so it's an overview of nutritional science. So that's my main teaching responsibility.
I also for the last ten or so years have had a big responsibility for administration. I direct an institute at the University of Minnesota called the Healthy Food, Healthy Lives Institute which focuses on the food and health and the integration of health science and agriculture because I am -- although I consider myself to be in allied health science,

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I'm in a college of agriculture. So we have a unique opportunity to bring together agriculture and food production with the -- with health and -- with human health. And so that's what my institute does, which I've been spending a lot of time directing for the last ten years.

Q. If I understood you correctly, you mentioned your research program involved human randomized controlled trials?

A. Yes.

Q. And what was your role in these randomized controlled trials?

A. Principal investigator. I have -- I have received grants for and been the principal investigator of seven or eight clinical trials. I was responsible for writing the protocol, in some cases working with colleagues on it, in some cases having almost the entire responsibility myself, in some cases leading a research team. But I've been in a leadership position with all of them, running the trials, supervising graduate students who would be interacting with participants, working with statisticians closely to analyze the data, writing -- writing the publications or supervising

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my students.

I -- as -- because I'm an educator, I -- it's very important to me that graduate students have experience writing publications. So even though in some cases it might be easier for me to write the paper, the students would write the first draft, and then I would work with them on many iterations until published so that I would feel that if my name's on the paper, then I can stand behind anything that's in it.

So I would say that my role in the trials that I'm talking about here has been very primary.

I've always done quite a bit of collaborative work with -- in which other researchers were the principal investigators on the clinical trial and I was a collaborator or a co-investigator and was involved in aspects of the study but not -- I did not have primary responsibility for the study.

Q. And in those studies that you played a collaborative role, what was your -- can you describe how you were generally involved in the study?

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A. I was involved as a member of the team. And so there would be, for example, conference calls periodically to discuss the trial. When the -- when the study -- in the beginning when the study was being designed, when the study -- when the grant was being written, I was involved and consulted about the writing of the grant, about the study design, about the endpoints that I was focused on, which were my area of expertise in relation to the study which was phytoestrogens and -- in -- in most of these studies and -- so that before the study, I was involved as a consultant in a way on the design. And I wasn't the driver, but I was part of a team. And then during the study, there were regular meetings to discuss how the study was going, problem solve, et cetera. And then I did not take primary responsibility for writing the publications, but I read and edited and was involved in the writing of all of the publications that -- that have my name on it that came from those collaborative studies.

Q. When you say you were a consultant in the design, did that include working on the protocol for the study?

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A. Yes. In particular, the part of the protocol that I was the most involved with.

Q. And what part would that be?

A. That would be the -- because -- I'm thinking of one study in particular which was a study of the effect of dietary soy constituents called isoflavones which are phytoestrogens, plant estrogens. The study was looking at the effects on bone health in -- in postmenopausal women and perimenopausal women in order to see if these exogenous phytoestrogens might prevent bone loss with aging. So I was the expert on phytoestrogens in that -- on that team. I was not an expert on bone. So the primary -- the principal investigator was an expert on bone, and so she knew how to design the study with respect to the bone endpoints, but I was an expert on how the supplement should be taken, how compliance should be evaluated, how the measurements would be made to determine what the levels were, et cetera.

Q. Did any of the trials that you worked on as part of your research program involve any aspect of cognitive function?

A. No.

Q. How about any of the classes

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you've taught? Did any of them involve cognitive function?

A. You know, I've done a little bit of work on cognitive function. I wrote a paper on food and mood many years ago, which is in my list of publications. I was asked -- I was asked to write that paper, and so I wrote a paper on it, and it was called food and mood, and this is many, many years ago. And in my classes, occasionally the subject of diet and cognitive function does come up. Diet and mental health, et cetera, for example, in my class that I teach Introductory Nutrition, the issue of the effect of micronutrients on mental health is something that we discuss. So it is something that I have -- I have had the opportunity to -- to look at, to think about, to talk about, to teach about in the context of nutrition as a small part of my work that I've done.

Q. And in writing that paper on food and mood, did you conduct research for it?

A. No, I didn't. That was a -- that was a literature review, so that was a review of what was known at that time.

Q. You also mentioned an institute

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that focused on food and health?

A. Yes.

Q. Can you -- did any of -- has any of your work for the institute involved cognitive function?

A. The work that I've done at the institute has involved cognitive function peripherally. So one of the things that I -- that I've done as director of the institute is to work with a local Native American tribe to host a conference on Native American nutrition. And we've held four of those conferences, and the fifth one is going to be held next May. It's a two-and-a-half-day conference with about 600 people coming from all over the country and Canada, some other countries as well. And there is a lot -- a great interest in the effect of food on mental health for Native Americans, the effect of trauma on -- on -- the effect of trauma on mental health and how that's affect- -- and how the loss of traditional foods has affected mental health.

So we've talked about mental health not cognitive function in the sense of detailed studies of cognitive function, but in a

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more general sense mental health. We've had speakers. We've had scientific sessions on those topics which -- which I've invited the speakers to and, et cetera, got to know the speakers well.

Q. So you've mentioned research program, your teaching, your institute while at the University of Minnesota. Is there any other work experiences in your position?

A. My position is primarily education, research, and then, of course, service or public engagement. And so I have done a lot -- quite a lot of service at the University of Minnesota. I've chaired many committees. I've chaired search committees for dean positions, for departments head positions, for faculty positions. I've been on the -- I am currently on the college promotion and tenure committee, which I've served on twice before, where we evaluate faculty to determine whether or not they deserve promotion and/or tenure. So I've been highly involved in that.

Some of my teaching -- I also for ten years was director of the nutrition graduate program. And in that capacity, I oversaw the entire graduate program. We had about -- I

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believe about 50 graduate students at that time, and I taught an introductory class to the graduate students in which we discussed good research practices, we discussed examples of fraud in science and how to avoid it and integrity in science and what the best way is to work with data to make sure that it is presented in the most objective, honest way. So -- and, of course, we critiqued papers in that -- in that class where the students would read research papers and we would go through and critique them. I would have this -- I would lead the students and -- and teach them. And then I would have them do presentations on topics so they got some experience putting presentations together. And then the other students in the class would question them and challenge them on different ideas.

Q. You mentioned earlier that you had funding for your research. You mentioned corporate sponsors, correct?

A. Yes.

Q. And who were those corporate sponsors?

A. I have gotten some funding early in my career from -- from -- can I -- is it okay

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if I look at my CV --
Q. Sure.
A. -- which we have up here? Okay.
Q. Yes.
A. Okay. So early in my career I received a grant from a company called Humanetics Corporation to -- it was a very small grant of less than $4,000 to look at the effect of a particular compound on DNA synthesis in mouse melanoma cells. So that was a very, very small in vitro study which was early in my career.
I also have more recently received funding through my work as director of the Healthy Food, Healthy Lives Institute from the Cargill Foundation, and that grant was an education grant, the purpose of which was to bring high school students to the university to introduce them to food and agriculture careers. It was a trial -- it's a -- it's a project, the purpose of which is to bring more diversity to food and agriculture which we have unfortunately an unacceptably low rate of -- of diversity within the field. And so the purpose of that study is to try to introduce students who might not think about it as a career to come to the university and

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get to know it a little bit. So that was from Cargill. Those are the only ones I can really see on my résumé.
I've also had some foundation support from the -- the Susan -- the Susan G. Komen Foundation and -- and then some -- a few other sources, state funds, et cetera. But as you can see from my CV, it's mainly federal funding.
Q. I believe you mentioned soy as one of the products that was involved that you focused on during your clinical research?
A. Yes.
Q. Are there any other products or ingredients that were -- that were involved in your research?
A. Yes. So I would say that for much of my career I focused on the health effects of soy consumption. I also have looked at the health effects of consumption and flaxseed and green tea extract. I was a collaborator on a project looking at omega-3 fatty acids and on another project looking at the interaction between soy and seaweed. And I've done a study looking at the interaction between soy and probiotics. So I've looked at probiotics as well in my own

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research. And then, as I said, the collaborative project was on soy and bone health, and I've done quite a few collaborative projects further looking at flaxseed.
Q. Have you ever conducted any research involving Prevagen?
A. No, I have not.
Q. Have you ever conducted any research involving apoaequorin?
A. I have not, no.
Q. Have you ever been involved in research involving vitamin D?
A. No, I have not.
Q. Your CV also mentions some work involving journals. Could you describe that, please?
A. I have acted as a reviewer for many, many scientific journals, nutrition journals. I am contacted a few times a month to review papers, so I've done quite a few peer review of manuscripts. In addition, I have served as a member of the editorial board for the Journal of Nutrition, which is one of the premier journals in nutrition, and the Journal of the Society of Nutritional Sciences, which is the American

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Society of Nutrition.
Currently I am -- I am an academic editor for another society journal called Current Developments in Nutrition which -- which is an open-access online journal of the American Society of Nutrition. And because of the work that I've done in Native American communities with scholarship involving work with triable communities, I helped launch a new section in that journal on the food and nutrition of indigenous peoples, and I'm the academic editor for that section. In that role, I supervise the peer review of any papers that come through on that topic. So I assign reviewers, I read their reviews, and I make the final decision about publication, whether or not the paper needs to be -- needs to be revised and whether or not the paper can be published.
Q. Okay. Have you ever been involved in any academic journals that focused on cognitive function?
A. No, I have not.
Q. Your CV also mentioned you were involved in some professional organizations. Could you describe that involvement, please?

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A. I've been involved with my main professional society which is, as I said, the American Society for Nutrition. I have served on the graduate education committee of that organization. I have served on a couple of different award committees. And I was -- last year, the year before, I was elected as a fellow of the American Society of Nutrition which is a limited group of people. It's not an automatic thing. Only about five to ten or so people per year are elected to be fellows of that society.

Q. Have you ever been involved any professional organizations that involve cognitive function?

A. I have not.

Q. And except for the article you drafted involving mood, have you ever been involved in any other articles that involve any aspect of cognitive function?

A. No, I have not to my knowledge. I don't recall any.

Q. In your professional career, have you ever evaluated someone's cognitive function?

A. No, I have not.

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Q. Do any of the articles listed on your CV involve vitamin D?

A. No, they do not.

Q. Dr. Kurzer, what areas do you consider yourself to be an expert in?

A. I'm an expert in nutritional science. This is what my Ph.D. is in. Nutritional science is a combination really of biochemistry and physiology as they apply to nutrients. And so this is my general area of expertise.

I teach basic nutrition, and so I'm in a position to keep up with the literature in nutrition and -- and so I would say that that's my general area of expertise.

I have more specific subareas of expertise which include dietary supplements, which include reproductive hormones and their interaction with -- with nutrition. I have done a great deal of work on the nutrition of women and gender differences and sex differences in response to nutrition, and that's another area of expertise for me. Cancer prevention is another subarea of interest to me.

So within the general area of nutritional science, I have these subareas of

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expertise. And then --

Q. Any other --

A. -- clinical -- clinical trials in nutrition. I consider myself an expert on that.

Q. Anything else?

A. Those are the main areas. Something else may come up again.

Q. So you don't consider yourself to be an expert in cognitive function, correct?

A. I -- in -- in my professional capacity, no.

Q. Do you consider yourself to be an expert in statistics?

A. I consider myself to be an expert in utilizing statistics in the -- in the -- in the context of nutrition studies. I've worked very closely with statisticians. I have -- I have not done very many statistical analyses on my own because I don't have a Ph.D. or formal training in statistics other than a series of classes that I took as a graduate student. So in every study that I have ever worked on, I've worked very closely with statisticians. I have never just handed the data over to them, asked them to

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analyze it and send it back to me. I always discuss with them various techniques, methods. We argue back and forth. I might recommend something else. They agree or don't and tell me why.

So I've been heavily involved in most of the statistical analyses for my research, although I would not say that I'm the primary driver. I'm the primary driver of the -- the -- the design of the study, the analytical work, the biochemical work, et cetera. But I work with others who have Ph.D.s in biostatistics.

Q. And I take it you've never done any research in the area of biostatistics?

A. That's correct, I have not.

Q. And have you ever taught any classes on biostatistics?

A. I have taught classes that included sections on biostatistics. So as a graduate student, I was a teaching assistant in a laboratory class in which we had the students do statistical analyses. And I recall having the students do an analysis of variance by hand. So they had to do all of the calculations by hand because it's -- it was extremely important to me, and it still is, that students who are in science

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don't -- don't use a sort of black box approach to the work that they do. It's very easy to just put data into a computer and it spits out the results, and the person doing it may or may not really understand what the program did. So it was very important to me in that capacity. And I've talked about it also in some of the seminars that I've taught as well and some of the graduate classes, the importance of actual looking at the data and understanding the data, not just putting it into a machine, getting the results out.

And -- and so the ideas of statistics and how they're properly used has been a thread throughout my career, something very important. So I've never taught a statistics course.

But in the context of all of the other things I teach, for example, in -- even in my introductory class I teach the students how to evaluate information because, as you can imagine, we are bombarded with so much nutrition information from the internet. Before computers, it was from magazines and newspaper articles and advertisements and radio and -- and so now it's computers. And students don't understand how to

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evaluate the data that they see, which one should they believe, this magazine article or this professor. And so I talk a little bit about statistical analyses and how important that is and how important it is to understand how to interpret statistics and how statistics can be interpreted in numerous ways. So I do talk about it in my courses, although it is not the primary focus of my teaching.

Q. Are you involved in any professional organizations relating to statistics?

A. No, I am not.

Q. Have you ever been involved in any academic journals that focus on biostatistics?

A. No, I have not.

Q. Earlier today we -- we -- you mentioned protocols in one of your responses. Could you describe what a protocol is?

A. A protocol is the detailed description of what is going to be done in an experiment. So in a protocol, the methods that are going to be used are described, the -- in a -- in a human study. There are many various things that could be described, including what the subject study population is going to be, inclusion

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and exclusion criteria, et cetera, how the data -- how the samples are going to be analyzed, what they're going to be analyzed for. If it's an animal experiment, how many animals there are going to be, et cetera. And so it's a -- it's a map. It's a map of how to go about doing the research.

Q. And what do people conducting the clinical trial use the protocol for?

MS. METZINGER: Objection to form.

You can answer, Dr. Kurzer, if you understand the question.

THE WITNESS: Okay.

The protocol is used, as I said, as a map, as a basic skeleton for conducting the study.

BY MR. WONE:

Q. And is RCT another -- an abbreviation from randomized control trial?

A. Yes. It is a randomized control trial, yes.

Q. And so today I'm going to use RCT as an abbreviation when I'm referring to randomized control trials.

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A. Okay. Sure.

Q. Did the RCTs you were involved in use protocols?

A. Yes.

Q. And would the RCTs you were involved in follow the protocol?

MS. METZINGER: Objection to form.

THE WITNESS: The RCTs that I've been involved in, the -- for the RCTs that I've been involved in, the protocols were written in the context of a grant application. And so they were written for the reviewers to understand what -- what we were going to do for purposes of decision about whether or not to fund the project. So we followed the protocol as best we could, but there are always changes to the protocol that happen during the clinical trial because the actual reality of what happens once you start may be slightly different from the theoretical framework that you've established. So that very often will

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vary from the protocol, the initial protocol.
BY MR. WONE:
Q. And when you varied from the initial protocol, were there any -- were there any future updates to the protocol?
MS. METZINGER: Objection to form.
THE WITNESS: Sometimes we would update the protocol, but we wouldn't necessarily have a -- we wouldn't have to report back to the funding agency. So there wasn't -- we -- we didn't have to have a formal document that was updated. That was not necessary and not required.
BY MR. WONE:
Q. Would you ever mention any of the changes that were made in the -- in the future -- in the later study reports?
MS. METZINGER: Objection to form.
THE WITNESS: If I considered them to be extremely important, I would mention them. But I would not

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necessarily mention other -- it would -- I -- it was my judgment to decide whether or not I thought it was substantive enough -- substantive enough to be mentioned. So it depended on the study and it depended on the variation from the protocol.
BY MR. WONE:
Q. Could you give an example of something you would consider substantive enough to warrant mentioning?
MS. METZINGER: Objection to form.
THE WITNESS: An example might be the study population in -- I have performed clinical trials in which it was very difficult to recruit participants, and so we had to expand our recruitment network from what we had originally proposed and we had to go to other clinics and other sites and use other mechanisms for recruitment other than what we had put in the protocol. And so we did report that.
When -- every year when I write

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an annual report to NIH for their -- for their records, one of the things that they ask is have there been substantive changes to the protocol, and I would put the change to the protocol in that report if it was substantive.
BY MR. WONE:
Q. So would a protocol from an RCT identify who the participants or who the study population would be?
MS. METZINGER: I'm sorry. Can you repeat that, Mr. Wone?
BY MR. WONE:
Q. Would an RCT protocol identify who the study participants would be?
MS. METZINGER: Objection to form.
THE WITNESS: Yes, the protocol will identify the study participants.
BY MR. WONE:
Q. And would the protocol describe the study design?
A. Yes, the protocol will describe the study design, but there are many, many levels

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of detail. So a protocol can describe it in much less design or in much less detail or much greater detail. So, for example, I've written grants where there was a page limit on the grant application, and so I was limited in what I could -- how much detail I could put in. So I had to select which -- which points I wanted to put into that protocol and which I would leave out.
Q. Did you ever write any protocols that were not for a grant -- in connection with a grant application?
A. I think that all of my protocols have been in connection to grant applications. And as I -- as I -- I would have to look in great detail at all of my studies, but I'm pretty sure that they were virtually all in relation to grant applications.
Q. So focusing on the instances where you didn't have a page limitation for the protocol, did those protocols provide details about the study design?
A. Yes. And -- and there's always a page limitation. So there's no such thing as no page limitation. Sometimes you have lots more pages than other times. But even for NIH where

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there is a greater page limit than for some of the other agencies, you're still -- you still have to keep your study design within -- within a small enough number of pages so that you can write the rest of -- the rest of what you need to write within the page limit. So the -- I -- I put as much detail as I can fit into that -- into that grant application.

Q. And the protocols you worked on, would they also describe the treatment that was being administered in the study?

A. Yes.

Q. And the protocols you've written for RCTs, would they also describe the measures that would be used to evaluate efficacy?

A. Yes.

Q. Would the protocols that you've written for RCTs also describe the screening criteria for participants?

A. Yes.

Q. And so there would be inclusion criteria?

A. Yes.

Q. As well as exclusion criteria?

A. Yes.

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Q. And would participants that don't meet the screening criteria be excluded from the studies you've worked on?

MS. METZINGER: Objection to form.

THE WITNESS: In general they would. But it's not always possible to make sure of that. I've had instances where, for example, I was recruiting postmenopausal women. And after I looked at the data and had measured hormones, I realized that some of them were not actually postmenopausal. And so they had to be eliminated from the data analysis because in the end it turned out they didn't fit the original criteria. So I analyzed the participants who fit what I was most interested in, but in recruiting I actually recruited other people as well.

BY MR. WONE:

Q. In the RCTs you've worked on, did the protocol describe the control?

A. Yes.

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Q. And what kind of details would it provide about the control?

MS. METZINGER: Objection to form.

THE WITNESS: I would say the detail about the control would be much less than the detail about the treatment. I might just have a sentence or two about the control being used.

BY MR. WONE:

Q. And in the RCTs you've worked on, would the protocol describe the blinding?

MS. METZINGER: Objection to form.

THE WITNESS: I would say that we don't necessarily describe the blinding. We say that it will be blinded but don't necessarily describe in detail what that -- how we're going to make sure that that happens. There is an assumption, I would say, that folks know what blinding means, and so we don't have to say in great detail this is exactly what we're going to do

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to make sure that things are blinded. We say it's going to be double-blind or single-blind, and that's really what we -- all we'd have to say. It's not necessary to describe it in more detail than that.

BY MR. WONE:

Q. For the RCTs you worked on, would the protocol describe whether there was any randomization used?

A. Yes.

Q. And would it describe how the randomization was to occur?

A. In some cases it would. I think for -- for an NIH grant where a great deal of detail is required, I would probably have put details about the kind of randomization that I was going to use. But I know that I've written other grants and I've written other protocols where I said that they were going to be randomized but not necessarily -- I didn't necessarily describe the technique that I was going to use to perform that randomization.

Q. In the RCTs you worked on, would the protocol describe the ratio of participants in

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the treatment group to the ratio of -- to the participants in the placebo group?

A. I'm not sure what you're asking, Mr. Wone. Can you maybe rephrase that a little bit? I'm not sure what --

Q. Sure.

A. -- you mean by "ratio."

Q. For example, if there was to be, you know, 4 to 2 or something like that, so 4 to 2 in terms of participants and treatment versus placebo and it wasn't just 1 to 1, is that something that the protocol would describe?

A. I have not done those kinds of studies. My studies have always had an equal number of people in each group.

Q. Have you ever used stratification in any of your RCTs?

A. Yes.

Q. And can you describe what stratification is?

A. Stratification is -- if -- if I'm understanding your use of the word, my interpretation of your -- of stratification is looking at particular groups of people. For example, if body weight -- if we think that body

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weight is an important co-variable, we might stratify the data on the basis of -- of obesity, let's say, you know, average of normal weight, underweight, overweight, or percentages of overweight, and we might look at the data differently in each of those groups because we suspect that the responses will differ on the basis of the participants belonging in those stratifications.

Q. And would the -- in the RCTs you worked on, would the protocol describe any stratification?

A. Sometimes they would. If we think about it in advance, we would say that the data will be stratified in this kind of way. But sometimes we decide to do that after the fact because while we're doing the trial, we realize that, you know, information -- information comes up during trials especially if they're long trials. I've done a trial that took five years. And it is very limiting to force yourself to stick to the knowledge that you had on that -- on -- during that week when you submitted that protocol. It's very important to use the most up-to-date, current information and be flexible. And so we

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have stratified data after the fact when we realized that this might be a variable that's very important to look at differently in -- you know, to see if the effect is different based on this co-variable.

Q. And when you stratified after the fact, was it after you analyzed the study data?

MS. METZINGER: Objection to form.

MR. WONE: I'll rephrase that.

BY MR. WONE:

Q. In the instances where you've stratified after the fact, was it after the study had concluded?

A. Yes, it was after the study had concluded because we don't usually -- we're -- we're so busy while the study is being conducted that all we can do is problem solve and deal with recruitment and making sure the subjects are compliant and collecting the samples. It's an enormous amount of work to conduct these clinical trials. And so we usually then think about the statistical analysis, yes, after the study is done. The data -- the samples may not have been

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analyzed yet. So if we're collecting biological samples such as -- such as urine or blood, et cetera, we don't necessarily have those data yet. But we think about -- we -- we think more deeply about the statistics before we perform them at the end of the study, and we may make some changes.

Q. And is stratification something you would discuss with the biostatistician that you worked with to analyze the data?

A. Yes, I would.

Q. Have there ever been any instances where you stratified the data after you had already started analyzing it?

MS. METZINGER: Objection to form.

THE WITNESS: I don't recall any. I'd have to look at the individual papers themselves and -- you know, because my career goes back 30 years. So I would have to really look at data to be able to analyze it, to be able to answer that question.

BY MR. WONE:

Q. If an RCT was going to have

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subgroups, is that something that would be identified in the protocol?

MS. METZINGER: Objection to form.

THE WITNESS: Can you rephrase that question, please?

BY MR. WONE:

Q. Sure.

If a study was going to focus on a particular subset of the entire study population, is that something that would be identified in the protocol?

MS. METZINGER: Objection to form.

THE WITNESS: It might be identified or it might not be because if it's something that we think about in advance, then it would be in the protocol. But if it's something that comes up during the conduct of the study which, as I said, could take a very long time, then it might be something that we decide to do after the protocol is written originally. And this is -- this is extremely

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important to remember, that clinical trials are incredibly expensive, incredibly difficult to do, and time consuming for many, many, many people. And so we try to get as much information.

My -- my green tea clinical trial cost $5 million or $6 million, and we felt that it was extremely important to try to get as much information from this population as possible. And so as information about the -- about green tea developed in the course of the study, things came up that we realized we could look at that we hadn't thought about in advance. And it would be, I think, neglectful to not pursue those additional opportunities.

BY MR. WONE:

Q. And the things that came up during the green tea study, was it while the study was ongoing or after the study had already concluded?

MS. METZINGER: Objection to

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form.

THE WITNESS: I would say both, that it could be -- some of it would have come up during the study and some of it might have come up after the study. But it would not have come up after we analyzed the data and looked at it and then decided, okay, now we're going to do some other additional things. This is something that would have come up before we knew what the primary results were.

BY MR. WONE:

Q. Okay. And would the study protocol -- strike that.

For the RCTs you worked on, would the protocols describe when the interventions were to be given?

A. Yes.

Q. And would the protocols describe how long the study period is going to be?

A. Yes.

Q. And would the study protocols state when the testing of the participants was to occur?

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A. Yes.

Q. And should the protocol identify the outcome measures being used to evaluate efficacy?

MS. METZINGER: Objection to form.

THE WITNESS: The protocol would identify the outcome measures as we saw them at the time of writing the protocol, but we very often would add and modify that as the study goes along as we realize that there may be other indicators of efficacy that we had neglected to put into the protocol that were important and would be very valuable information to have. So we might modify that -- those.

BY MR. WONE:

Q. And if you were to modify the -- the measures, is that something you would consider to be a substantive change and would later report to an NIH report?

A. Yes, I would add that we have expanded our aims to include additional questions and additional endpoints.

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Q. And after -- if after the study had started, before you analyzed the data you were to -- you mentioned you sometimes change the stratification. Is that also something you would consider a substantive change to be reflected in a -- in an NIH report?

MS. METZINGER: Objection.

MR. de LEEUW: Objection.

THE WITNESS: I would not necessarily put that in an NIH report, but it would go into the results of the study and when I report the results. But I wouldn't feel a need to put that kind of a change into an interim report to NIH, an annual report, no. They don't care about that kind of stuff. They're not that interested in it. They wouldn't -- they're -- they're more interested in -- you know, that I accomplish what I initially said that I was going to.

BY MR. WONE:

Q. And if you were to make any changes to the subgroups that -- that weren't in the original protocol, is that something you would

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consider a substantive change and would include it in an NIH report?

MS. METZINGER: Objection to form.

THE WITNESS: No, I would not -- I would -- again, I would -- that would be part of the results that we reported. But it would not be considered a change in the study design.

BY MR. WONE:

Q. For the RCTs you've worked on, did the protocols include a statistical analysis plan?

A. Yes.

Q. And have there ever been any instances where you made any changes later to the statistical analysis plan?

MS. METZINGER: Objection to form.

THE WITNESS: There may have been. I really don't recall at the moment. Again, I'd have to look at my work in great detail to be able to answer that question.

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BY MR. WONE:

Q. And would you consider a change to how you analyze the data to be a substantive change?

MS. METZINGER: Objection to form.

THE WITNESS: It depends on what the change is. I can't make a blanket statement on that.

BY MR. WONE:

Q. Have you ever heard someone describe a change being made to an RCT as post hoc?

A. Yes.

Q. And what is your understanding of what post hoc means in that context?

A. Post hoc is -- my understanding of the use of the term "post hoc" in this context is that it is analyses that are done that were not planned, preplanned, that were decided after the study was -- was complete.

Q. Do you believe it's important to distinguish when an analysis has been predetermined versus post hoc?

MS. METZINGER: Objection to

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form.

THE WITNESS: I think it depends on the context. There are situations in which it's important because of the -- for example, if you're submitting a paper to a very, very rigorous journal, they might insist on that kind of clarification. But certainly there are many studies, many, many, many studies published that do not declare if an analysis is post hoc or not. So, you know, it really depends on where the publication is going to be and what the context is.

BY MR. WONE:

Q. And do you know why those rigorous publications insist on identifying a particular change as post hoc?

MS. METZINGER: Objection to form.

THE WITNESS: I believe that it's because in the strictest sense of using statistics, when statistics are interpreted very narrowly and strictly, that it is considered best practice to

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identify what your hypothesis was up front and what you might have changed or added afterwards in order to avoid the perception or -- that a -- that a researcher might be doing what might be called data mining, et cetera, which is not considered good practice.

But there are many, many, many researchers who do not necessarily declare if something was post hoc and they are not data mining. There is no data mining. They are with good conscious and with great integrity, they are realizing that there are other endpoints that are important, and so they report on them, which I think in many cases and in most cases is good practice.

BY MR. WONE:

Q. When you are evaluating a study, how do you know what the results are, the product of data mining versus someone who had found something new?

MS. METZINGER: Objection to form.

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THE WITNESS: Very often it's not -- it -- it -- I don't believe it's always possible to tell. There may be researchers who -- who do data mining and publish papers and don't -- you know, and they don't say anything about it. And so I suspect that it's done quite a bit and we don't -- we just don't know about it.

BY MR. WONE:

Q. In the context of an RCT, are you familiar with the term "statistically significant"?

A. Yes.

Q. And what does it mean when the results of an RCT are statistically significant?

A. A p-value is -- is chosen, and usually the p-value is .05. And if a statistical test is performed which shows that the -- that the product that you're studying or the treatment is effective at the level of .05, it achieves significance, that means that there's only a 5 percent chance that the results were due to random effects. So it's a -- it's a mathematical technique to determine probability -- the

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probability that your results are true versus they occurred by chance.

Q. And when evaluating clinical studies, is statistical significance something you look for?

A. Yes, it is. But it isn't the only thing I look for. I look for statistical significance along with other things as well.

Q. And what are some of those other things? What are the other things you look for?

A. I always look at the data. I always, with my own studies, graph the data so that I can see exactly what's happened in a visual reputation, and I always look at trends. And the reason I always look at trends is because in human studies, there are so many variables affecting outcomes, many of which we don't know.

So we control for the variables that we know about. But there are many, many, variables that we don't know about because we're discovering new ones all the time.

So you can see in studies, for example, in population studies, epidemiological studies, the data may be controlled for five to ten different variables that they think may be

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affecting the endpoint. And there are many that we don't know about.

And so the -- everything is stacked against our ability to see a true result. It's very, very difficult in human studies, in clinical studies as opposed to in vitro studies or animal studies where you can, you know, lock these creatures up in a box and control everything in their environment.

With humans, particularly if they're free living, there are so many things that we can't control that it's very, very difficult to get a highly significant, statistically significant result.

So in my opinion and the opinion of a number of my colleagues and many statisticians who I've work with, it is important to talk about trends because sometimes you may not be -- you may not have enough statistical power to achieve significance. But if the trends of a number of endpoints are in the same direction, that -- that is meaningful and that is worth reporting.

MS. METZINGER: Mr. Wone, we've been going for just about an hour and a

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half. I don't need to take a break at this moment, but I think we should think about taking one in the next few minutes if you get to a natural point.

MR. WONE: Yeah, I've got a couple more questions. But, yeah, we can take a break after that.

MS. METZINGER: Okay. Thank you.

BY MR. WONE:

Q. When you're looking at data, how do you weigh the trends versus data that's statistically significant?

MS. METZINGER: Objection to form.

THE WITNESS: That's a difficult question to answer because statistical significance, of course, is considered the sort of, you know, kind of proof in a way to some degree. But in my opinion, it's very narrow. The choice of .05 is an arbitrary choice. And even statisticians will agree to that. And the American Statistical Society agrees that .05 is -- is an arbitrary

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cutoff. Why not .01 or why not .1?

I have worked with statisticians who did a lot of clinical trial work who told me that they felt that for clinical studies a p-value of .1 or .2 even should be used because of all of the variability that makes it so difficult to get a statistically significant result with a .05 cutoff.

So, therefore, I consider the -- the showing of trends to be very, very important, and I very often will report trends along with significance.

So I can't say that one is more important than the other or that one would invalidate the other. I would look at them together. And I would look at the p-values and the trends in the context of the p-values and, you know, if -- if there are p-values that show no -- many -- if there are -- if my statistical analysis shows across the board nothing but then I show some trends, depends on how strong the trends are. If the trends are weak

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trends, then I wouldn't value them as much as I would strong trends. If the trends occur with a number of endpoints, that would be more valuable than if the trends occur with just a couple of endpoints.

So, again, it's looking -- it's standing back and looking at the whole picture. That's how -- that's my approach to working with data, is that I -- I try not to be very narrow and try to be a little bit more broad in my thinking and -- in what I present.

BY MR. WONE:

Q. Do you use a p-value of .05 in your research?

A. Yes, I do. I use a p-value of .05 because that is the -- the most widely accepted p-value. But my way of dealing with that is to show trends. So I don't change the p-value because I have no way of knowing what I should change it to. It's all arbitrary.

Q. And in the context of an RCT, have you heard the term "clinical significance"?

A. Yes.

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Q. And what is your understanding of what clinical significance means?

A. Clinical significance as opposed to statistical significance refers to the -- the importance with respect to health, disease, and the biological endpoints that you're talking about as opposed to the significance of the numbers on paper.

Q. Is it possible for something -- for a result to be statistically significant but not clinically significant?

MS. METZINGER: Objection to form.

THE WITNESS: Yes, it is. It is possible. It's certainly possible, but I would qualify that by saying that there are very often arguments about that among clinicians so that there might be some clinicians who would say it's an important result and others who say that it's not clinically significant. So, yes, that does occur.

BY MR. WONE:

Q. And what camp do you find yourself falling in? Do you believe that every

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change is clinically significant?
MS. METZINGER: Objection to form.
THE WITNESS: I am not an expert on -- I'm not a clinician myself. I'm not an expert on clinical significance, so I wouldn't be able to comment on that.
BY MR. WONE:
Q. And so in the research that you've conducted, how do you determine whether the statistically significant results were clinically significant?
MS. METZINGER: Objection to form.
THE WITNESS: It hasn't always come up in my research, but there have been a few times when it has come up. And in that -- in those times, I often have clinical collaborators who help me interpret the clinical significance of -- of the result.
BY MR. WONE:
Q. So if I remember right, you did some research focusing on endpoints related to

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cancer?
A. Yes.
Q. And so if there was an issue of clinical significance, you would consult with someone who has -- who considers himself an expert in cancer? Is --
A. Yes.
Q. -- that what you mean?
THE WITNESS: Yes.
MS. METZINGER: Objection to form.
THE WITNESS: But -- but I wouldn't -- I must -- I must say -- I must add to that, Mr. Wone, that that isn't something that I consider to be necessary. Very often there are not clinicians who are part of research teams and papers. Data can be published, and then it's up to the readers to reach their own conclusions. And so readers then have the opportunity to interpret the significance, the clinical significance of the results.

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BY MR. WONE:
Q. So you would publish the data without saying one way or the other whether you thought it was clinically significant?
A. That's right. That is exactly right. I wouldn't always talk about the clinical significance. And most scientists -- many scientists do not. And then that becomes a topic for conversation in the scientific community.
Q. When you were conducting your RCTs on endpoints involving cancer, why did you choose to use human clinical trials rather than animal studies?
A. Honestly, for me, I mean, this is -- I know this is not what you're asking, but I have much more fun with human clinical trials than I do with animal trials. Personally, I don't like killing animals, and so I've never done -- I'm a little bit unique as a scientist in that I've not spent a good portion of my career working on animal studies just because -- I think they're extremely important and they provide very, very critically important data, but personally, I -- I don't want to -- I don't want to chop the head off a rat, you know, and put it in a guillotine, which

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is what is done. So I don't do it.
But I also think that clinical trials are important. It's -- it's very important in -- in many situations, not all situations, to have verification of results in humans because the results of animal studies may or may not be extrapolatable to humans. So I appreciate the importance of doing human studies.
Q. And would the same be true versus for human studies versus in vitro studies, the result from an in vitro study may not be -- it may not apply to humans?
A. Yes.
Q. And would you agree that if you wanted to make a claim about a product having an effect in humans, that you would need human clinical trials?
MS. METZINGER: Objection to form.
THE WITNESS: That actually depends on the situation. I think very often I would agree that human trials are needed, but there are situations in which you can't do human trials. So, for example, with tobacco, with tobacco

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effects, it wouldn't be considered ethical to have two groups one of which smokes -- one which you give cigarettes to and the other one you don't.

Or cancer trials. It would not be considered ethical to take two groups of people, give one group cancer and the other group no and then see what happens.

So there are situations in which it's either not ethical, not feasible too expensive. And, frankly, I think that because of the expense of clinical trials of -- especially the very big clinical trials, they're going to be funded less and less. And, in fact, in -- when you look at NIH funding, they have been funded less and less, and there's more and more research going into developing animal models and alternative models to working with humans because they're so impractical and -- and difficult and expensive to do.

MR. WONE: Well, we certainly

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don't want to give cancer or heart attacks to anyone.

Okay. I think we can take a break here, if that's fine with you, Jaclyn.

MS. METZINGER: Sure, that would be great.

MR. WONE: Okay. We'll go off the record.

THE VIDEOGRAPHER: We are going off the record at 10:09 A.M.

(Off the record from 10:09 until 10:28.)

THE VIDEOGRAPHER: We are going back on the record at 10:28 A.M.

BY MR. WONE:

Q. Hello, Mr. Kurzer.

A. Hello.

Q. I just wanted to go back to something we had talked about before the break. Is it possible to have an RCT investigating whether a dietary supplement causes change in memory in humans?

MS. METZINGER: Objection to form.

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THE WITNESS: Yes, it is.

BY MR. WONE:

Q. When were you retained by the defendants as an expert, Dr. Kurzer?

A. I'm not sure how to answer that. I've been retained for over the course of a number of years because there have been various cases dealing with this issue. So my original -- I was retained originally probably about maybe five to seven years ago. I don't know exactly. I'd have to look it up to see.

Q. And when you were retained five to seven years ago, was it in connection with this case or something else?

A. In connection with -- with -- I guess I'm -- not being a lawyer, I'm not sure how specific about the case that you want to be there. There's been some litigation. There's been -- I have met with the FTC about this previously. I met with some commissioners previously maybe for -- or a few year -- two to three years ago, I think, so -- so there have been -- it's all been related to the same issues but in different contexts as far as the litigation goes.

Q. Have you ever done any work for

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any of the defendants that was not related to litigation?

MS. METZINGER: Objection to form.

THE WITNESS: I'm not sure how to answer that. I -- I don't believe that I have. But, again, I don't understand the technical legal terms, so I'm not exactly sure what the answer to that is.

BY MR. WONE:

Q. Have you ever done any research for the defendants?

A. Yes.

Q. What kinds of research?

A. I've done literature reviews as summarized in the report that I've written.

Q. Any other kind of research?

MS. METZINGER: Objection to form.

THE WITNESS: I believe that all of my research is summarized in the report.

BY MR. WONE:

Q. Have you ever had any

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communications with any other experts that have been retained by defendants in this case?
A. I have not.
Q. Did you review any of the reports by any of the other defendants' experts?
A. Yes, I have.
Q. Do you recall which reports you've reviewed?
A. I reviewed, I believe, all of the other reports, Dr. Goodman, Dr. Schwartz, I think. I can't -- I've read the FTC reports and the -- the defendants' reports. And so I'm not recalling offhand whose name is which.
Q. Okay.
A. But I believe I've read them all.
Q. Okay. Aside from attorneys representing the defendants, have you ever had communications with any other person relating to your work in this case?
A. No, I have not.
MS. METZINGER: Your audio is not coming through, Mr. Wone.
MR. WONE: Okay.

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BY MR. WONE:
Q. Have you ever interacted with anyone affiliated with Quincy Bioscience?
MS. METZINGER: Objection to form.
THE WITNESS: I don't believe I have. It's possible that someone from Quincy was at the FTC meeting. I don't recall. But that would have been the only interaction, was at that meeting. I have not had other interactions.
BY MR. WONE:
Q. And does your report, what's been marked as Exhibit MK1, contain a complete statement of all of the opinions you're offering in this case?
MS. METZINGER: Objection.
THE WITNESS: Yes. All of the opinions that I was asked to offer at the time that I wrote my report are present. I may have other opinions in addition to that that aren't in the report.
BY MR. WONE:
Q. Did anyone assist you in writing the report?
A. No. I wrote the report myself.
Q. And the other opinions that you have you mention that were not in the report, are they opinions that you intend to offer that are going to be offered in this case by defendants?
MS. METZINGER: Objection.
THE WITNESS: They would be opinions that I would offer if I'm asked a question related to them. If I'm asked a question related to something that's not in my report, I will offer the opinion.
BY MR. WONE:
Q. In connection with your work in this case, did you review any advertising for Prevagen?
A. I did, yes.
Q. Do you recall which ads you reviewed?
A. I recall reviewing the -- the label in particular. And that's the main thing I can recall right now. I may have reviewed other things, so you may have some documents that if you'd like me to look at them, I can -- I can look at them.
Q. Okay. Have you ever been involved in the marketing of Prevagen?
A. I have not, no.
MS. METZINGER: Objection to form.
BY MR. WONE:
Q. Do you consider yourself an expert in marketing?
A. No, I do not.
Q. Do you consider yourself an expert in advertising?
A. No, I do not.
Q. If you'd please go to paragraph 8 of your report which has been marked as Exhibit MK1.
A. Yes, I see that right here, paragraph 8.
Q. And does paragraph 8 identify the claims for Prevagen that you evaluated in this case?
A. Yes.
Q. And in paragraph 9, you state that the defendants provided you with a definition of competent and reliable scientific evidence,

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correct?
A. Yes.
Q. Aside from this litigation, is that definition, a competent and reliable scientific evidence, something you use to determine about -- in other -- sorry. Strike that.
Aside from this litigation, have you ever used the definition of competent and reliable scientific evidence?
MS. METZINGER: Objection to form.
THE WITNESS: I have used that in other situations in which I've written expert reports.
BY MR. WONE:
Q. Have you ever used that definition, "a competent and reliable scientific evidence," outside of the litigation context?
A. No, I have not.
MS. METZINGER: Objection to form.
BY MR. WONE:
Q. Instead of the definition of competent and reliable scientific evidence in

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paragraph 9 of your report, if I said the human -- that competent and reliable scientific evidence meant human clinical testing that was randomized, double-blinded and placebo-controlled conducted by qualified researchers, would it still be your opinion that the claims are supported by confident and reliable scientific evidence?
MS. METZINGER: Objection to form.
THE WITNESS: Could you repeat that question, please, Mr. Wone?
(Reporter read back requested material.)
MS. METZINGER: Note the objection again.
THE WITNESS: I'm not comfortable answering that question because you're creating a hypothetical that doesn't exist. So if you'd like to ask that question in another way, you know, that -- that isn't quite so hypothetical, I'd be happy to answer it.
BY MR. WONE:
Q. I'm going to refer to the claims

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that you listed in paragraph 8 as the "challenged claims," which is the abbreviation that you used. Okay?
A. Yes.
Q. Do you believe there's human clinical testing that was randomized, double-blinded placebo-controlled and conducted by qualified researchers to support the challenged claims?
MS. METZINGER: Objection to form.
THE WITNESS: Yes, I do.
BY MR. WONE:
Q. If you could please go to paragraph 10, Doctor. It's on the next page, page 3 of your --
MR. de LEEUW: You have to keep your voice up. You have to keep your voice up. I don't know if you can adjust your microphone, but --
MR. WONE: Sure.
MR. de LEEUW: -- sometimes you fade out.
MR. WONE: I'll try to move it closer.

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BY MR. WONE:
Q. Paragraph 10 of your report --
A. Yes.
Q. -- MK1 --
A. Yes.
Q. -- you state in this -- in this paragraph that you conducted a literature search on the general topic of cognitive function as well as the affects of apoaequorin/Prevagen and vitamin D3 on brain function and memory.
Do you see that?
A. Yes, I do.
Q. So the first search you -- if I'm understanding right, was the first search you did on the general topic of cognitive function?
A. That's correct.
Q. And how did you perform this literature search?
A. I used a database at the University of Minnesota in which I put in keywords related to cognitive function, dementia, mild cognitive function, Alzheimer's disease, et cetera, and looked at papers related to that in order to provide a background and context for the report.

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Q. Was "memory" one of the search terms you used?
A. Yes.
Q. Do you recall the name of the database?
A. The database I usually use is Ovid, O-V-I-D. Very similar to PubMed.
Q. And did anyone assist you with your literature search?
A. No.
Q. And did you review all of the results from your search?
A. Yes, I did. I reviewed the relevant results, right? So I might have gotten hundreds of papers, and I reviewed the ones that were the most relevant to what I was writing.
Q. And did your search terms include cognitive decline?
A. I don't recall, but I think probably I did, cognitive function, memory, dementia. I may have had cognitive decline in there, but it would have been picked up by the other words.
Q. And your second search was on the effects of apoaequorin/Prevagen?

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A. Yes.
Q. Okay. And how did you conduct this literature search?
A. Using the term "apoaequorin," seeing -- seeing what else is out there in the literature.
Q. And did you use the same -- the same database, Ovid?
A. Yes.
Q. Were there any other search terms besides apoaequorin?
A. You know, I -- I don't have a record in front of me of what search terms I used, but I probably used apoaequorin, brain, memory, cognitive function, et cetera.
Q. And did anyone assist you with this literature search?
A. No.
Q. And did you review all of the articles that you believed to be relevant?
A. Yes.
Q. And how about your search for vitamin D? What search term did you use for that?
A. Vitamin D and then various forms of vitamin D. I would have put in there brain,

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memory, cognitive function, Alzheimer's, dementia. Those kinds of terms would have been in there.
Q. And it was also done -- the vitamin D search was also done with the same database, Ovid?
A. Yes.
Q. And did anyone assist you with the vitamin D --
A. No.
Q. -- literature search?
A. Nobody assisted me, no.
Q. And did you review all of the results from the vitamin D -- vitamin D literature search that you believed to be relevant?
A. Yes.
Q. And do you know whether the vitamin D literature search included cognitive decline?
A. It probably did, but I'm sure that I used "mild cognitive impairment" as a search term and "cognitive function" and "memory." Those would have all picked up a paper on cognitive decline.
Q. You previously stated that you don't consider yourself to be an expert in

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cognitive function. How do you know that the studies you found in your literature search represent the current view among experts in cognitive function?
MS. METZINGER: Objection to form.
THE WITNESS: The way that I know is that I'm a very, very well-trained, experienced scientist, and I'm able to evaluate data outside of my area of expertise. I often have to do this for grant applications, for writing up of publications, et cetera. I never have the luxury of just staying within a very narrow area.
And so I explained before that one of the things that I have taught in my career is I've taught students how to interpret data, how to interpret papers. They aren't necessarily published in the exact area of expertise of the person who is reading them. So a person who is experienced at clinical trials, for example, has to be able to interpret and understand

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animal studies and in vitro studies even though that may not be where they put most of their time and energy in their own work. It is basic understanding of science.

I also understand how to evaluate the quality of journals, the quality of authors of journals, and the quality of -- of papers from the study design, et cetera.

So I believe that I am very qualified to evaluate the current understanding about cognitive function despite the fact that I don't have a Ph.D. in a related science.

BY MR. WONE:

Q. Did anyone assist you in analyzing the results of your literature search?

A. No.

Q. If you could turn to page 37 of your expert report which we marked as Exhibit MK1, please. And when I say "page 37," I'm referring to the pages that are printed at the bottom of the document, not the page number in the -- in the AgileLaw viewer.

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A. Okay. Yes.

Q. And is page 37 the first page of your bibliography of your report?

A. It is, yes.

Q. Does this bibliography contain sources that you found through your literature search?

A. Yes, it does.

Q. Aside from documents related to the Madison Memory Study, did you include any other documents on your -- in your bibliography that did not come from your literature search?

A. I included some of my own publications as references to comments that I made about my experience in my introduction to my -- in my introductory paragraphs.

Q. Okay. Anything else?

A. I don't believe so. Well, I may have -- no, I believe that this is all from my literature search. I think that I may have been -- I may have been provided with some unpublished papers by the attorneys representing the defendant, but I don't recall if I referenced them in the bibliography.

Q. Did you rely on those

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unpublished papers as the basis for any of the opinions in your report?

A. The only unpublished paper that I relied on was the reanalysis of the Madison Memory Study data because the publication evidently had some errors in the data analysis, and so it was redone. And there was a subsequent paper written which I did rely on because I wanted to use the most current, accurate results.

Q. Okay. And do you recall what the errors were in the original publication?

A. You know, I don't recall. There were some statistical errors, I believe, and so I didn't really go into great detail with the attorneys about exactly what they were, but that they -- but that I -- I did trust that when they gave me the reanalyzed data, that that was accurate.

Q. So the opinions about the Madison Memory Study in your report are based on the Lerner reanalysis?

A. Yes.

Q. And to clarify, I don't know if we covered it, when I said "Lerner," do you know who that is?

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A. I believe it's Kenneth Lerner, the author of the papers, yes.

Q. Okay.

A. I know the name.

Q. Okay. And he was the -- he was the principal investigator for the reanalysis, correct?

A. Yes.

MS. METZINGER: Objection to form.

BY MR. WONE:

Q. Okay. If we could turn to section 4 of your report, please, Exhibit MK1.

A. What page would that be?

Q. If you'll give me second, I will let you know.

I believe it starts on page 4 of your report.

A. Okay. I see it.

Q. Section 4 titled "Cognitive Function and Its Measurement"?

A. Yes.

Q. Are the opinions expressed in this section based on the results of your literature search?

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A. Yes.
Q. Are they based on any other experiences you've had in your career?
A. No. They're based on the literature search.
Q. And that's all on Section 4, correct?
A. Excuse me? Can you repeat that?
Q. The -- all -- when you said it's based on your literature search, you're referring to all of Section 4, correct?
A. Yes. Let me look at the... Yes.
Q. Okay. How about Section 5 of your report? It's on page 6. Is Section 5 also based solely on your literature search?
A. Yes, it is.
Q. In paragraph 28 of Exhibit MK1, also on page 6, do you see a mention of the Cogstate?
A. Yes.
Q. And what is your understanding of what Cogstate is?
A. Cogstate is a group of tests that test various aspects of cognitive function.

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And my understanding is that it's been validated and that it is listed in the NIH database of acceptable cognitive testing techniques.
Q. Have you ever used the Cogstate in any of your research?
A. No, I have not.
Q. Have you ever reviewed any journal articles -- strike that.
Aside from this case, have you ever reviewed any journal articles that used the Cogstate?
A. Not in great detail. I did -- I remember looking at the literature to get a feel for when Cogstate has been used in other situations to make sure that I was confident that this is something that's been used in other -- in other published papers, and I did find that it had been used. So that was not something that I -- that I cited in the -- in the report, but I remember that I did look into that.
Q. Okay. So did you also do a literature search on Cogstate?
A. I believe that I did, yes, for just for that purpose. It was really just to get a feel for the -- whether or not it had been used

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in other situations. I wanted to make sure of that.
Q. Okay. And did anyone assist you in the literature search regarding Cogstate?
A. No.
Q. If you could go down to paragraph 30 of your expert report.
A. Yes.
Q. The first paragraph of Section 6.
A. Yes.
Q. And do you see the first sentence were you're just starting with "both in vitro"?
A. Yes, I see that sentence.
Q. And so in reviewing the evidence in this case, you reviewed in vitro studies related -- involving apoaequorin, correct?
A. Yes.
Q. And would any of the in vitro studies that you reviewed show that Prevagen improves memory in humans?
A. No, there would not be that direct connection. What the in vitro studies show was that apoaequorin is neuro protective in a --

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in a situation in which the tissue has been removed. So it's not in a living human. It's in tissue in a cell culture model.
Q. And do you know whether the -- sorry. Strike that.
The tissue that was used in the in vitro studies was not human tissue, correct?
A. I think that it -- that is correct, but I'd have to see the paper because I have -- you know, I have 150 or 160 references here, so I'd have to -- if you want to show me the paper, I can look at it. But my recollection is that it was not human brain tissue.
Q. Okay.
A. But I'm not certain of that.
Q. Okay. I'm showing you what's been marked as Exhibit MK2.
(Marked Exhibit MK2.)
BY MR. WONE:
Q. Do you see that, Dr. Kurzer?
A. Okay. I'm sorry. MK2. Yes.
Q. Is that the -- is that the research article you were citing to when you discussed in vitro studies?
A. Yes, it is.

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Q. And did the research in Exhibit MK2 involve human cells?
A. No. It was a rat brain slice preparation.
Q. And do you agree that the effects seen in the study in a rat brain cell may not be the same in a human cell?
MS. METZINGER: Objection to form.
THE WITNESS: I would say that the rat results may be the same in a human or may not be. We don't know.
BY MR. WONE:
Q. Okay. Going back to -- if you could go back to Exhibit MK1.
A. Yes.
Q. Paragraph 30 again.
A. Okay.
Q. Do you see in that paragraph you mention animal studies?
A. Yes.
Q. Do you agree that the animal studies cited in paragraph 30 do not show that Prevagen improves memory in humans?
MS. METZINGER: Objection to

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form.
THE WITNESS: I would -- I would say that the animal -- the canine studies prove that Prevagen exerts this function in canines. And in this situation, I would trust the data to apply to humans quite a bit more than with rats because canines are considered an excellent model for human brain function.
The structure of the brain in canines is very similar. Canines experience age-related cognitive decline. Canines have a lot of human behavioral characteristics. And, in fact, human drugs are used in canines. For example, antidepressants. Prozac is used in canines successfully.
So canine -- the canines brain is thought to be an excellent model for the human brain. And so in this case, although it is not -- you could not conclude -- conclusively say that these results show that the same thing would occur in humans, I do believe that the

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data are very, very strongly suggestive because the model is so close to the human brain.
BY MR. WONE:
Q. What do you mean when you say "strongly suggestive"?
A. That's a very -- it's -- that's kind of a subjective comment. What I mean is that I would expect that these results would be confirmed in human studies. I would expect that to be the case. In the case of rat studies, in my opinion, it could go either way. But in this situation, because of these results and because of the similarity of brain function and structure between canines and humans, I would expect that the same thing would occur in humans.
Q. Do you agree that humans are not biologically identical to canines?
MS. METZINGER: Objection to form.
THE WITNESS: I do agree that humans are not biologically identical to canines. I also agree that humans are not biologically identical to each other. There's a certain amount of

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variability even between humans.
But, yes, of course canines and humans are not biologically identical, but the genetic makeup, as I'm sure you know, of -- of canines and humans are large -- have an enormous amount of overlap.
BY MR. WONE:
Q. And do you know whether we would -- whether the effects seen in the Milgram study would happen in humans over the same duration and dose?
MS. METZINGER: Objection to form.
THE WITNESS: Can you repeat your question, please, Mr. Wone?
BY MR. WONE:
Q. Sure.
Do you know whether the effect that was seen in the Milgram study would happen in humans when you -- considering the same duration and dose?
A. I do not know that for certain. I would expect that to be the case, but I certainly did not know that for certain because

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the study was done in canines.
Q. I've marked and introduced what's been labeled as Exhibit MK3.
(Marked Exhibit MK3.)
BY MR. WONE:
Q. Do you see that, Doctor?
A. I do.
Q. And is this one of the documents you analyzed for your report?
A. Yes, it is.
Q. And is this the Lerner reanalysis that we discussed earlier?
A. Yes, it is.
Q. I've marked another document which has been labeled as Exhibit MK4.
(Marked Exhibit MK4.)
BY MR. WONE:
Q. Do you see that, Doctor?
A. Yes, I do.
Q. And is this another document that you reviewed in connection with the -- in connection with your report?
A. Yes, it is.
Q. And is Exhibit 4, MK4, the analysis that you said had errors?

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A. Yes, it is. I was told that.
Q. You were told that by the -- by the defendants' attorneys?
A. Yes.
MS. METZINGER: Objection to form.
And, Dr. Kurzer, I would just caution you not to divulge the substance of any communications that you've had with counsel.
THE WITNESS: Thank you.
BY MR. WONE:
Q. If you would go to paragraph 33 of your report, please, Exhibit MK1.
A. Yes.
Q. In the first sentence, you wrote, "After initial publication in the Madison Memory Study results, it was discovered that transforation and dataset errors had been made in the data analyses."
Do you see that, Doctor?
A. Yes.
Q. And that's your understanding of -- of the errors that were in Exhibit --
A. Yes.

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Q. -- MK4?
A. That's correct.
Q. You mentioned that the reanalysis was done by Georgetown Economic Services in paragraph 33. Do you see that?
A. Yes.
Q. And were you involved in any way in this reanalysis?
A. I was not.
Q. Have you ever had any interactions with anyone affiliated with Georgetown Economic Services?
MS. METZINGER: Objection.
Dr. Kurzer, again, I would caution you not to divulge the substance of any communications that you may have had with Georgetown Economic Services to the extent that counsel may have been involved in those communications.
THE WITNESS: Okay.
Best that I don't answer the question, I guess.
BY MR. WONE:
Q. Well, I'm not asking for the

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substance of the communications. I'm just asking now whether you've had any interactions with anyone affiliated with Georgetown Economic Services.
A. You know, actually, honestly, I don't recall. I may have, but I don't recall.
Q. Have you ever had any interactions with someone named Howard Beales in connection with your work in this case?
A. What's the name?
Q. Howard Beales.
A. Howard Bealed. I don't believe so.
Q. Beales.
A. Spelled, please.
Q. B-E-A-L-E-S.
A. Beales. I don't believe so.
Q. And were you involved in any way with the Madison Memory Study?
A. I was not.
MS. METZINGER: Objection to form.
BY MR. WONE:
Q. Have you ever spoken with anyone who was involved with conducting the Madison

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Memory Study?
A. I don't believe I have.
Q. Have you ever had any interactions with anyone involved in analyzing data from the Madison Memory Study?
MS. METZINGER: Objection to form.
And, again, Dr. Kurzer, I would just caution you not to divulge the substance of any communications that you have had with counsel. If you can answer Mr. Wone's question without doing so, you're free to answer the question.
THE WITNESS: Okay.
Mr. Wone, can you repeat the question, please?
BY MR. WONE:
Q. Sure.
Have you ever had any interactions with anyone who was involved in analyzing the Madison Memory Study data?
A. I don't believe so.
Q. Okay. I'm introducing what has been marked as Exhibit MK5.

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(Marked Exhibit MK5.)
THE WITNESS: Yes.
BY MR. WONE:
Q. Do you see that, Dr. Kurzer?
A. I do.
Q. And have you seen this document before?
A. I have.
Q. And could you describe what Exhibit MK5 is?
A. MK5 is a protocol, I believe, for the Madison Memory Study.
Q. And who is listed as the principal investigator for the Madison Memory Study?
A. KC Lerner is listed.
Q. And based on this protocol, what was the Madison Memory Study's population?
MS. METZINGER: Objection to form.
THE WITNESS: The study population on this protocol is adults between the ages of 40 and 95, 100 adults between the ages of 40 and 95.

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BY MR. WONE:
Q. I'm sorry. I missed it. What was the last part of your response, Dr. Kurzer?
A. 100 adults between the ages of 40 and 95.
Q. Thank you.
When the Madison Memory Study was conducted, do you know how many participants were in the study?
A. I believe they recruited over 200 people.
Q. In your experience, is it common to recruit more than double the population for a given study?
MS. METZINGER: Objection to form.
THE WITNESS: I don't believe it's common, but I believe that it does happen. There are many reasons why investigators might want to do so.
BY MR. WONE:
Q. And do you know why the -- why the investigators in the Madison Memory Study recruited over 200 participants?
A. I don't know their reason.

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Q. [redacted]
MS. METZINGER: Objection to form.
THE WITNESS: [redacted]
BY MR. WONE:
Q. And what did -- sorry. Strike that.
[redacted]
A. [redacted]
Q. [redacted] **specific Cogstate measures to be used?**
A. No, it doesn't.
Q. In your experience, is it good methodological practice to not identify the specific measures to be used in a study in the protocol?
MS. METZINGER: Objection to form.

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THE WITNESS: I don't think that it's -- I can't really comment on that. I think there were many reasons -- and there are many situations in which investigators will speak more generally in a protocol rather than very specifically.

So, for example, I could imagine writing up a protocol in which I say that I'm going to be measuring estrogen metabolites without listing the exact ones that I'm going to be measuring. So I don't think it's -- it is good practice or bad practice. I think it is practice that I've seen before.

BY MR. WONE:

Q. In the protocols you worked on, have you had protocols where you didn't list -- didn't identify the primary efficacy variables?

MS. METZINGER: Objection to form.

THE WITNESS: No, I would say that I have identified the primary efficacy variables, but there are degrees of detail that I may or may not

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have gone into in describing them.

BY MR. WONE:

Q. And is that because when you're drafting your protocols you -- you always have page limitations?

A. It's page limitations. Also the methodology that I'm using. I might not be certain which of them I'm going to be able to analyze, you know, chemically what's going to be practical, et cetera. And so there are various reasons why I might not go into as much detail.

And some protocols would -- you know, in some situations if I'm writing a protocol for an organization like NIH, they might have certain requirements of their own regarding the detail. But I wouldn't say that it is broadly accepted that every protocol has to go into a certain amount of detail. There's variability in that, and that's accepted, widely accepted.

Q. When you say "widely accepted," you mean -- what do you mean? By who?

A. I mean, I see it all the time in -- in scientific -- in grants that I've reviewed, in -- in papers that are -- that are reporting on protocols on study design where they -- the whole

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paper is describing the study design. They may or may not go into great detail. Of course in the results, they then will list exactly what they were evaluating. But in the message section, they -- there are variations in the amount of detail that people go into.

Q. Do you know whether the investigators in the Madison Memory Study had any space limitations in drafting their protocol?

A. I do not know.

Q. Do you know which Cogstate measures were used in the Madison Memory Study?

A. I -- I don't -- I know that there were eight or nine different -- different measures, and I'd have to look at the paper to be able to name them all. But I -- you know, I did look at them very closely.

Q. So if you'd like to refer back to Exhibit MK3.

A. Okay.

Q. Does Exhibit MK3 identify the Cogstate measures that you believe --

A. Yes.

Q. -- were used in the Madison Memory Study?

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A. Yes, it does. In table 1, it lists nine different tests that were used.

Q. And do you know whether there are any other Cogstate measures that were used in the Madison Memory Study that are not included in table 1?

A. I don't recall.

Q. In table 1 of Exhibit MK3, there's two columns, correct?

A. Yes.

Q. One labeled "Task," the other one labeled "Cognitive Domain Measured"?

A. Yes.

Q. Is it your understanding that the column under Cognitive Domain Measured identifies which domain corresponds to a specific task?

A. Yes, I -- that's my understanding.

I also understand that there's tremendous overlap among these, that they're not entirely discrete. Discrete memory is not entirely independent and separate from executive function. Verbal learning obviously requires memory. So there's tremendous overlap among

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these, but I do agree and understand that they are thought to represent primarily these particular cognitive domains.

Q. And is it your understanding -- what is your understanding that they're not -- that the cognitive domains are not discrete based on?

MS. METZINGER: Objection to form.

THE WITNESS: It's based on my evaluation of the literature and reading general papers that discuss cognitive function and measurements of cognitive function and what contributes to memory and what factors contribute to memory and what memory is important for.

So in the background reading that I -- that I did, which was significant for this, it was very clear that these are -- have enormous overlap. Plus, there are a number of -- of studies and there are a number of publications that state very clearly that these measures are not

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independent.

BY MR. WONE:

Q. And you're referring back to publications or information that you obtained from your literature search that we --

A. Yes.

Q. -- discussed earlier?

A. Yes.

Q. If we could go back to Exhibit MK5.

A. Okay.

Q. What is the investigational product identified in Exhibit MK5?

A. Well, the -- in the title, it states Prevagen apoaequorin dietary supplement.

Q. So Prevagen is the product being studied in the Madison Memory Study?

A. That's correct. Yes, here we go. Prevagen 10 milligrams.

Q. And did the protocol in Exhibit MK5 discuss how the data from the study would be analyzed?

MS. METZINGER: Objection to form.

THE WITNESS: There is a brief

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description of the statistical analysis on page 5.

BY MR. WONE:

Q. Did the protocol identify the specific statistical test that would be used to analyze the data?

MS. METZINGER: Objection.

THE WITNESS: It did not.

BY MR. WONE:

Q. Did the protocol in Exhibit MK5 identify how the data would be analyzed?

MS. METZINGER: Objection to form.

THE WITNESS: If you mean does it describe the specific statistical tests that will be used, it does not.

BY MR. WONE:

Q. Did the protocol identify whether the tests would be analyzed separately or collectively?

MS. METZINGER: Objection to form.

THE WITNESS: I don't believe that it does.

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BY MR. WONE:

Q. [redacted]

MS. METZINGER: Objection to form.

THE WITNESS: [redacted]

BY MR. WONE:

Q. Do you know whether subgroups were used in the Madison Memory Study?

MS. METZINGER: Objection to form.

THE WITNESS: I don't believe that subgroups were used in the sense that they analyzed the group that they were intending to analyze. They -- the intent of the study was to look at healthy people, and so they analyzed the AD 0-2 group, which was a group that I focused on, because that was the intent of the study. So they over-recruited. And in the recruitment, they included additional

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people. But when they did the statistical analysis, they did it on the population which they were aiming to study at the beginning of the study.

BY MR. WONE:

Q. Were all of the participants in the Madison Memory Study in the AD8 0-2 group?

A. No, they were not.

Q. And what is -- what do you mean when you say "AD8"?

A. That's the -- the -- the Alzheimer's disease screening form which has eight questions related to changes in memory over time. And if there are eight questions and if someone says yes to all eight saying that they've had changes and problems with all eight areas of memory, then that would be viewed -- an 8 or 7 would be viewed as, you know, severe dementia.

0-2 is viewed where you just have nothing you answer yes to or maybe you answer yes to one or two of the questions. That would be considered normal cognitive decline with aging or possibly mild cognitive impairment. But basically healthy people would be in the -- in my opinion, healthy people would be in the 0-2 on the AD8

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form.

Q. And prior to reviewing the Madison Memory Study, were you familiar with the AD8 tool?

MS. METZINGER: Objection to form.

THE WITNESS: I was familiar with it, yes.

BY MR. WONE:

Q. Have you ever used the AD8 in your own research?

A. I have not.

Q. How did you become familiar with the AD8 tool?

A. My mother had dementia, and so I -- I learned about it in the context of her clinical experience, just from my family personal experience.

Q. Okay. Have you ever used the AD8 tool in your professional work?

A. I have not.

Q. Is the AD8 tool mentioned in the protocol that's in Exhibit MK5?

A. It's not.

Q. [redacted]

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[redacted]

A.

[redacted]

Q.

[redacted]

A.

[redacted]

Q. And would somebody who scored a 3 on the AD8 tool have significant neurological disease?

MS. METZINGER: Objection to form.

THE WITNESS: My understanding is that the -- at the level of AD8 3, it is the beginning of more severe cognitive dysfunction. Therefore, a

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cutoff of 2 is the appropriate place to differentiate healthy people from people who are beginning to develop more serious dementia and cognitive dysfunction.

BY MR. WONE:

Q. So if somebody is beginning to develop, does that mean they have a history of significant neurological disease?

MS. METZINGER: Objection to form.

THE WITNESS: Yes, in the sense that patient has a history, could be synonymous with patient has existing significant neurological disease.

So the history implies long in the past, but my interpretation of this is patient has a history of significant neurological disease means we don't want to recruit people with significant neurological disease. And history is used often -- it's a medical term, and it's often used in these protocols. But what we mean is existing.

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BY MR. WONE:
Q. And what is your basis for the -- your interpretation of what significant neurological disease means?
A. Can you rephrase that question, please, Mr. Wone?
Q. Sure.
How do you know -- so you've given me your interpretation of significant neurological disease and what you think it means, correct?
MS. METZINGER: Objection.
THE WITNESS: I don't have -- I'm not exactly sure what you're asking. I understand that -- that AD8 0-2 is the categorization of people who are generally healthy and that once you get to 3 and above, you're moving into the territory of people who have more than normal aging cognitive decline and more than mild cognitive decline. And this I know from the reading that I've done from the literature review.
BY MR. WONE:
Q. And do you know whether the

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investigators of the Madison Memory Study had the same understanding of what significant neurological disease means in Exhibit 5, MK5?
A. I assume yes. I assume that they had the same understanding. It seems to me to be fairly obvious.
Q. Did the protocol mention in Exhibit MK5 -- sorry, strike that.
Did the protocol in Exhibit MK5 mention any interim analysis?
A. I don't believe that it did, no.
Q. And in your experiences conducting RCTs, is an interim analysis something you would include in a protocol?
MS. METZINGER: Objection to form.
THE WITNESS: Not necessarily, no. In fact -- in fact, in the green tea trial that I did, the clinical trial with a thousand participants who consumed green tea for -- for a year, green tea supplement for a year, we did not state in the protocol that we were going to do an interim analysis, but we decided to, to do an interim analysis.

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And in our case, it was to look for adverse events, to make sure that there weren't any adverse events. And so we did do an interim analysis even though it was not stated in the protocol. And that was approved by the data safety and monitoring board and it was approved by NIH. It was not a problem that it was not in the original protocol.
BY MR. WONE:
Q. And so you reported the interim analysis to NIH when you --
A. Yes.
Q. Correct?
A. Yes. Yes.
Q. Do you know whether any interim analysis was done in the Madison Memory Study?
A. I believe that they did do some interim analyses after -- possibly after 30 days and 60 days in addition to the final reported analysis on day 90.
Q. And do you know whether those interim analyses were related to safety or looking for adverse events?

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A. I don't believe so. I believe that they were looking for efficacy. And in many clinical trials, that -- it's -- it's -- it's not uncommon to do an interim analysis to look at efficacy because in the case of very important drug studies, for example, if something is found to be efficacious partway through the study, they might be so -- feel that this is such an important finding that they feel like the study should be stopped and the drug should be, you know, moved to approval. So it's not unheard of to do interim analyses for efficacy as well as for adverse events.
Q. And in those situations when the interim analysis is performed, would it be later discussed in the study report?
MS. METZINGER: Objection to form.
THE WITNESS: Not necessarily. In fact, we published -- for the green tea trial, we published at least two papers on adverse events, and I don't believe that we talked about the interim analysis in either one because it was more of -- you know, it was not

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something that we felt was a primary endpoint, and so it was not in the final publication.

BY MR. WONE:

Q. Could you explain that further? What was not considered the primary endpoint?

A. The interim -- the results of the interim report. So in the case of the green tea trial where we did an interim analysis of adverse events, we didn't feel that it was necessary to put that interim analysis in the final report because what was of most interest to people reading the report are the final results.

Q. And did you find any adverse events in that green tea trial?

A. We found minimal adverse events. We found some, but not enough to -- to be viewed as a problem by FDA or NIH.

Q. Would you describe -- would you agree that the results of the Madison Memory Study were related to cognitive function?

A. Yes.

Q. And would you agree that those results were the primary focus of the Madison Memory Study?

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A. Yes.

Q. And is it your -- is it your understanding that the interim analysis looked at efficacy related to cognitive function?

MS. METZINGER: Objection to form.

THE WITNESS: I believe that they did. But I think that the primary interest was what happened at the end of the study. So in the report, the focus was on the end of the study. And I have done studies where I analyzed endpoints during the study, but the report focused on the end-of-study data because that's what is of most interest. And when you write a publication, you don't want to flood the reader with so much stuff that it's going to be difficult for them to get the main gist of what you're trying to say.

So there's a balance between being -- being honest and having integrity and presenting what you found and at the same time not putting so

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much stuff into the -- into the -- into the report that it's really hard to read and difficult to -- for the reader to understand what the most important thing is.

BY MR. WONE:

Q. But you agree that the Madison Memory Study's interim analysis related to the primary interest of the study?

A. Yes. Oh, excuse me. I'm sorry. Can you repeat that question? I'm not sure I heard it correctly.

MR. WONE: Could the court reporter please read that back.

(Reporter read back requested material.)

THE WITNESS: I -- I need to -- to change my response on that. I think that it related to it in the sense that it was focused on the same endpoints of -- that -- that reflect cognitive function. But I don't think that the 30-day or 60-day endpoints were the primary interest for the reader. I think that the 90-day end of study

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endpoint would be the primary interest.

BY MR. WONE:

Q. Did the protocol mentioned in Exhibit MK5 state whether the Madison Memory Study was blinded?

A. Yes, it said it was blinded.

Q. And did the protocol in Exhibit MK5 describe how the blinding was done?

A. No, it did not describe it. And I would be surprised if it did. It's -- it's not common for researchers to put in the protocol exactly what the mechanism of blinding is going to be. You know, there are many, many methods of blinding, and I'm not familiar -- I think that it's -- it's more detail than is of interest to most either reviewers or -- or, you know, grant reviewers, manuscript reviewers, et cetera. It's not usually put in. That's -- that's -- that's drilling down very, very into the weeds, in my opinion.

Q. Okay. Going back to the AD8 for a moment, do you know how the AD8 was administered in the Madison Memory Study?

A. The AD8 was administered to the prospective participants.

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Q. And did the participants complete the AD8 tool themselves?
A. I believe that they did, yes.
Q. Do you agree that it's preferable to have the AD8 administered with an informant?
MS. METZINGER: Objection --
THE WITNESS: Yes.
MS. METZINGER: -- to form.
THE WITNESS: Yes. I -- I -- I know that I have read that is it preferable to have it administered by an informant, but I have also read that in instances where that is not practical or possible, it is acceptable to have it administered directly to the participant.
BY MR. WONE:
Q. And do you know in the case of the Madison Memory Study whether it was possible to have the AD8 administered through an informant?
A. I do not know that.
Q. Do you know whether it was practical in the Madison Memory Study to have the AD8 administered through an informant?

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A. I do not.
Q. Do you agree that the results of the AD8 when administered directly to the participant may not be as reliable versus when it's administered through an informant?
MS. METZINGER: Objection to form.
THE WITNESS: I believe that the reliability is thought to be best when administered by an informant, but at the same time it doesn't mean that it's unreliable when administered to the participant.
BY MR. WONE:
Q. A few moments ago you mentioned that the AD8 0-2 was the group of primary interest, correct?
A. Yes.
Q. I wanted to ask, what was -- what was your basis of that understanding?
A. The basis of that understanding is my reading of the protocol which states that they want healthy people and not people who have -- who are exhibiting neurological symptoms coupled with my understanding that interpreting

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the -- the AD8 -- interpretation of the AD8 is such that the 0-2 group is what would be considered the healthy population without significant neurological changes.
Q. What would be the difference between the 0-1 group versus the 0-2 group in terms of neurological condition?
MS. METZINGER: Objection to form.
THE WITNESS: My understanding is that the 0-1 group would be viewed as having no cognitive dysfunction, and the 0-2 group might include some people with some very mild cognitive dysfunction.
BY MR. WONE:
Q. Did the protocol in Exhibit MK5 discuss randomization?
A. I believe that they say that the subjects will be randomized, but they don't describe in detail how that will be. I'm glancing through it right now, so -- to try to better recall.
Yes, they do say that -- that it is randomized. They say in the methodology that

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the participants will be randomized.
Q. Did the protocol state how the randomization would be done?
A. The protocol did not state exactly how the randomization would be done. And this is extremely acceptable, in my opinion. There are many ways to do randomization. It can be done by computer. It can be done by a number of different programs. You can Google randomization and there are websites that will help you randomize. You can pick names out of a hat to randomize. There are lots of different ways. And it would be very unusual for the principal -- the -- the investigators to describe exactly what their method of randomization is. Usually saying "randomized" is good enough for us when we're reading a protocol or a paper.
Q. And did the -- did the protocol in Exhibit MK5 discuss stratification of the participants?
A. No, they did not. But as I said, I don't believe that the participants were stratified in the sense that the group that they analyzed, the 0-2 group, in my opinion, was the group of interest from the start. So I don't

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think this is a stratification in the sense that we were discussing before.

Q. If the 0-2 group was the group of interest, do you know where the Madison Memory Study included participants outside of that group?

MR. de LEEUW: Object to the form.

THE WITNESS: I do not know that. I do not know that. But there are many possible reasons that would be completely legitimate.

BY MR. WONE:

Q. Does the protocol in Exhibit MK5 identify the ratio of participants in the treatment versus placebo groups?

A. No, they don't.

Q. And do you know how the participants with AD8 scores of 0, 1, and 2 were distributed between the placebo and treatment groups?

A. I don't recall. I would have to look at the paper. Ratio 3 to 2 is the -- is they reported.

Q. And do you know whether that 3 to 2 ratio was in place at each of the AD8 levels,

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so 3 to 2 ratio at 8D8 0 and 3 to 2 ratio AD8 1 and a 3 to 2 ratio at AD8 2?

MS. METZINGER: Objection to form.

THE WITNESS: I do not know. I don't think that they stated that. I'm looking at the study design right now. I don't believe they said any -- I don't believe that they commented on that.

BY MR. WONE:

Q. And would you expect that the 3 to 2 ratio would be consistent across each of the specific AD8 levels?

MS. METZINGER: Objection to form.

THE WITNESS: I would not require that or expect that. I think it would be good if the ratio was met what they were -- what they were looking for within the group of interest, which is the 0-2. So that's where I would want this 3 to 2 applied within the 0 to 2 group. I wouldn't be as concerned with the rest of the

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population.

BY MR. WONE:

Q. If the treatment and placebo groups are not following the 3 to 2 ratio at each specific AD8 score, could that affect the study results?

MS. METZINGER: Objection to form.

THE WITNESS: Can you rephrase the question, please, Mr. Wone?

BY MR. WONE:

Q. Sure.

So you testified you don't know whether the 3 to 2 ratio was in place at each of the specific AD8 0, 1, and 2 levels, correct?

A. That's correct.

Q. And would it affect -- could it affect the results if there were different numbers of participants at each of those levels between the treatment of placebo groups that didn't follow the 3 to 2 ratio?

MS. METZINGER: Objection to form.

THE WITNESS: In looking at table number 2 in Exhibit -- in

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document MK3, you can see that in the AD8 0-2 group that ratio is followed. And that is the place where I would want it to be followed because I believe that that is the main outcome of interest. The main outcome of interest is the AD8 0-2. So that's where that ratio would need to be applied.

BY MR. WONE:

Q. But it's your understanding that there could be different numbers of AD8 1 in the treatment and placebo groups that are not following the 3 to 2 ratio at that specific score, correct?

MS. METZINGER: Objection to form.

THE WITNESS: I'd have to take out my calculator and do a calculation, but the 0-1 group is listed right next to it. And there are 24 in the placebo and 37 in the apoaequorin, so the ratio may be slightly different in the 0-1 rather than the 0-2. But you can see that it's very -- there are more in the

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apoaequorin, significantly more.
BY MR. WONE:
Q. No. I was asking about just AD8 1, for example. In the 0-2 group, do you know whether the 3 to 2 ratio was followed for participants with AD8 1?
MS. METZINGER: Objection to form.
THE WITNESS: Tell me if I'm -- if I'm misunderstanding you, but if you look at table 2 on page 5, the right-hand side has AD8 0-1.
BY MR. WONE:
Q. So I'm not including the 0. I'm just asking --
A. I see. I see.
Q. -- specific level.
A. I see. 0 -- rather -- just -- just the level 1.
Q. Yes.
A. From the paper -- from the paper, it is not apparent what the ratio was for each individual level of 0, 1, 2, 3, 4.
Q. Okay. And could it affect the results if the ratio was not the same at each

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specific level within the AD8 0-2 group?
MS. METZINGER: Objection to form.
THE WITNESS: I don't know if it would affect the results. I really can't comment on that. I think it's possible that it would. It's possible that it wouldn't. And, you know, there were many other things that could affect the results too. So personally I'm not concerned about that.
BY MR. WONE:
Q. Is it your understanding that Cogstate measures when given at baseline indicated the participant's level of cognitive function?
A. Yes.
Q. And would you expect in the Madison Memory Study for the participants AD8 scores to be correlated with their performance on the Cogstate measures at baseline?
MS. METZINGER: Objection to form.
THE WITNESS: Maybe you can clarify that question for me because you're asking a statistical question by

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using the word "correlation." But I think maybe you're asking something that's a little bit more general than a statistical question which is could the baseline value influence how they respond later. Is that what you're asking?
BY MR. WONE:
Q. I'm asking whether -- would you expect -- here, I'll rephrase. Hold on a second. Would you expect the people who did better in the AD8 -- well, I should qualify. Would you expect the people who are lower scores in the AD8 measure to do better in Cogstate tests at baseline?
MS. METZINGER: Objection to form.
THE WITNESS: I think that that's possible. They probably would. And that's why it was important for them to compare baseline values on Cogstate between the placebo and the treatment group. And you can see on table 2 when you look at the AD8 0-2 group, there is no difference at

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baseline in -- in the scores that they have on the tests. So that is important.
And I also believe that they took baseline into account in their data analysis so that they -- they used baseline as a co-variable so that that was taken into account because that is important.
BY MR. WONE:
Q. Did you look at any data to see how participants in the Madison Memory Study did on the AD8 scores versus how they did at Cogstate tests at baseline?
MS. METZINGER: Objection to form.
THE WITNESS: I don't recall that they did that comparison or that they reported it.
BY MR. WONE:
Q. And it wasn't something that you looked at?
A. No.
Q. Do you know when the Madison Memory Study began?

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A. I believe that it began in 2009.
Q. And do you know when it ended?
A. 2011.
Q. I think you've said this before, how long was the Madison Memory Study?
MS. METZINGER: Objection. Form.
MR. WONE: Sorry. I'll rephrase that.
BY MR. WONE:
Q. What was the study period in the Madison Memory Study?
A. The entire study took 90 days.
MS. METZINGER: Mr. Wone, we've been going for about another hour and a half. I just wanted to get a sense of when you think you might want to take the next break.
MR. WONE: I've got a handful of questions more, and then I think we can break for lunch.
MS. METZINGER: Okay.
MR. WONE: Is that okay?
MS. METZINGER: That's fine with me.

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Dr. Kurzer, does that work for you?
THE WITNESS: Absolutely.
MS. METZINGER: Thank you.
BY MR. WONE:
Q. Okay. I've introduced and marked Exhibit MK6.
(Marked Exhibit MK6.)
BY MR. WONE:
Q. Do you see that, Dr. Kurzer?
A. Yes, I do.
Q. Does this document, MK6, relate to the Madison Memory Study?
A. Yes, it does.
Q. Does Exhibit MK6 mention an interim analysis?
MS. METZINGER: Objection to form.
THE WITNESS: It talks about preliminary data.
BY MR. WONE:
Q. And what -- what is the year depicted on the document in Exhibit MK6 in the first paragraph?
MS. METZINGER: Objection to

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form.
THE WITNESS: I'm sorry. Can you rephrase that question, please, Mr. Wone?
BY MR. WONE:
Q. Sure.
What is the year depicted in the first sentence or the first paragraph of Exhibit MK6?
A. What is the year depicted?
Q. Yes. Yes.
A. 2010.
Q. So if the study was still being conducted in 2010, is it possible for an investigator to analyze preliminary data without breaking the blinding?
MS. METZINGER: Objection to form.
THE WITNESS: The blinding has to be broken, but there are ways to do it that secures the blindness of the study, and we did that in the green tea trial. What you do is you have a statistician who's not intimately involved with the study do the analysis

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so that the investi- -- the real purpose of blinding isn't so much to blind the investigators of -- of preliminary results, it's to blind investigators to which person is on which treatment. That's what you don't want the investigators or the people to know. And interim unblinding can be done in a way in which the investigators are kept blinded to who is taking what.
I'll tell with you the green tea study, when we did that, it was enormously frustrating for me because I desperately wanted to know, you know. But nobody could know until the end of the study. We -- the participants wanted to know. They were emailing us and saying "I think I'm on this because I'm having these effects." We could -- we had no idea. Until the very end of the study we had no idea. In fact, we didn't unblind the study until, you know, after -- you know, after we had the results in terms of us knowing

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which person was on which treatment.
That's the real purpose of blinding, and it's very -- it's entirely possible to maintain that even with an interim analysis.
BY MR. WONE:
Q. And do you know whether those safeguards to prevent that were done in the Madison Memory Study?
A. I don't know. I assume that they were because they say that it was a blinded study. So my assumption when reading it is that they did it properly and did not unblind it to them -- to the -- to the people who were working with the participants, interpreting the data, et cetera.
Q. But you haven't reviewed any documents to inform you as to how the blinding was broken for the preliminary --
A. No.
Q. -- analysis?
A. I do not -- right, I have not seen any documents --
MS. METZINGER: Objection to form.

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THE WITNESS: -- related to that.
BY MR. WONE:
Q. Does the document in Exhibit MK6 mention the AD8 0-1 subgroup?
A. They do not mention the -- the AD8 subgroup. They do say in the second paragraph that Prevagen is a new tool for staying cognitively fit, which to me means that the people in the study started out cognitively fit. I think that's the main point.
In this kind of a press release, it would be way more detail than people would be interested in to hear something about AD8 0-2. They'd have to then explain what that means. That's -- that's something that is more appropriate for a much more detailed scientific report. For this kind of thing, you would not expect to see that.
Q. Do you know whether the data that's reported in Exhibit MK6 was from a specific subgroup?
MS. METZINGER: Objection to form.
THE WITNESS: I do not know for

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sure. But as I said a few minutes ago, because they talk about staying cognitively fit, my interpretation of this is that the people in this study started out cognitively fit.
BY MR. WONE:
Q. So the data that's depicted could be from the 0-2 group, right?
A. Yes.
Q. It could be also from the 0-1 group --
A. Yes.
Q. -- right?
And it also could be some other -- some other group, correct?
A. Correct. And this is -- this is -- this is not a scientific report, so I would not expect the level of -- of rigor that you might expect in a scientific paper. I just -- you just wouldn't.
Q. And if the procedures that you discussed earlier to maintain blinding during a preliminary analysis were not -- were not followed, would that affect how you would interpret the results?

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MS. METZINGER: Objection to form.
THE WITNESS: Can you rephrase that question, please, for me?
BY MR. WONE:
Q. Sure.
Earlier you discussed procedures that -- that an investigator could use to maintain blinding during a preliminary or interim analysis, right?
A. Yes.
Q. And so if those procedures were not followed, would it affect how you interpret the result?
MS. METZINGER: Objection to form.
THE WITNESS: You know, it would depend. You -- I -- it might or it might not. There are levels of rigor that vary across studies. And I think that applying this very, very high level of rigor that I would say applies to a drug trial or an NIH-funded study is just not appropriate for this kind of dietary supplement that the -- I --

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my understanding is that the FTC guidance allows for much more flexibility in interpretation of research used to substantiate claims.

And so, you know, I would be much more concerned about some of the things that you're talking about and some of the things that you've asked me about if this was a drug trial and with -- with very serious implications, very serious cost if -- if there are errors, very serious health -- adverse health events if there are errors, et cetera.

But for something that's safe and is a nutritional supplement meant to supplement the body's intake of food, I just wouldn't be nearly as concerned with some of the kinds of things that you're asking me about as -- as -- as you might be -- as I would be if it were a drug trial.

I know that's not exactly a direct answer to your question, but, you know, I just wanted to say that

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because you're asking me about interpreting and would I be worried about this.

And, you know, if -- if -- if they had unblinded themselves in this study, that might be a little bit of a concern, but it can still be a very, very well-done study. In fact, I think that requiring blinding is a very extreme requirement that, in many cases, is not necessary in -- in -- on a level of scientific rigor and accuracy that blinding -- the study would -- the results would still be accurate if the study were blinded.

BY MR. WONE:

Q. Would you describe the RCTs that you've conducted in your career as being methodologically rigorous?

MS. METZINGER: Objection to form.

THE WITNESS: I think that they have, but they have not all been blinded. So, for example, the soy protein studies that I've done, you

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can't blind soy protein. There isn't something else that you can give that is not identified -- not -- that cannot be distinguished. Soy protein has a flavor. People who are take -- drinking a soy protein drink, no. And so in my soy protein studies, we -- we've used casing milk protein as the control. And neither we nor the participants were blinded. They knew. We didn't tell them, but they knew because they could taste the difference. So they knew if they were consuming the soy. And that was really the only way to do the study. There isn't -- when you're doing a study with foods, there isn't a way to blind the participants and -- or the -- or the researchers. And yet, I think it's still a very rigorous -- it was still a very -- those are still rigorous studies published in very, very good scientific journals having gone through extensive peer review.

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BY MR. WONE:

Q. And those studies that didn't have blinding, the lack of binding was part of their design. That was how they were designed, correct?

A. Yes. We knew in the beginning that they wouldn't -- that it wouldn't be blinded.

Q. And the RCTs you worked on involved health claims for nutritional supplements, correct?

MS. METZINGER: Objection to form.

THE WITNESS: The RCTs that I've worked on and the clinical trials that I've worked in -- on that weren't -- that weren't necessarily blinded have involved the effect of dietary constituents which could be considered supplements, but soy protein isn't exactly a supplement, but it's a -- it's a food constituent on various health endpoints.

BY MR. WONE:

Q. You've also worked on RCTs that were blinded and did involve a dietary supplement?

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A. Yes, particularly the green tea study that I was talking about. In that case, we gave pills, and the pills for the placebo and the treatment group were identical, and they were blinded and we were blinded.

Q. And would you agree that blinding -- double-blinding is something that's possible with a dietary supplement like Prevagen?

MS. METZINGER: Objection --

THE WITNESS: Yes --

MS. METZINGER: -- to form.

THE WITNESS: -- it is.

BY MR. WONE:

Q. I'm sorry. I didn't hear your answer, Doctor.

A. Yes.

MR. WONE: Okay. I think we can go off the record.

THE VIDEOGRAPHER: We are going off the record at 12:15 P.M.

(Off the record from 12:15 until 1:01.)

THE VIDEOGRAPHER: We are going back on the record at 1:01 P.M.

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BY MR. WONE:

Q. Good afternoon, Dr. Kurzer.

A. Good afternoon, Mr. Wone.

Q. I'd like to go back to some things that we talked about earlier this morning.

A. Sure.

Q. If you could go back to your report, what's been marked as Exhibit MK1 --

A. Yes.

Q. -- paragraph 33, please.

A. Yes. I have it here.

Q. Do you see in the second line where you discussed the initial publication that it was discovered that transformation and data set errors had been made in the data analysis?

A. Yes, I see that.

Q. I was wondering what -- what do you mean by "transformation"?

A. I don't know what the exact problem was. This is a very long time ago and I -- I don't recall getting into the details about it. There -- the way that the data were analyzed I guess involved some kind of transformation, and I'm not sure what the transformation was. And that was caught later on. So I really can't

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answer that. I'm sorry.

Q. Do you have any recollection as to what the data set errors were?

A. No, I don't. I don't remember. I think I -- I think we talked about it. I may have talked about it at the time, but I just don't remember right now.

Q. Did you review any documents that would have told you what those transformation or data set errors were?

A. No, I did not.

Q. Earlier this morning, it's my understanding, you testified that it's your belief that Prevagen is intended for healthy older adults; is that right?

A. Yes, it is.

Q. And so if Prevagen is intended for healthy older adults, when you were conducting your literature search, why did you use the term "Alzheimer's"?

A. Why did I use the term "Alzheimer's." Because sometimes cognitive decline and cognitive function is evaluated in a larger setting in which Alzheimer's is also evaluated. So I wanted to pick up the broadest

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number of papers that I could. I wasn't interested in Alzheimer's as an endpoint, per se. But the purpose of a literature review is to pull in as many papers as you can and then select from them the ones that you think are the most appropriate.

Q. And would that also be the reason why you included dementia in your literature search?

A. Exactly. I wasn't sure how much I would get from just looking at cognitive function or cognitive decline because what you get from a literature review is dependent upon the keywords that the authors of the papers put in, and so sometimes you miss things because the key word isn't exactly right. So that is the reason.

Q. And if Prevagen is intended for healthy older adults, why did you discuss Alzheimer's disease in paragraph 25 of your report?

A. The reason I discussed it is because Alzheimer's disease is the -- the end of the spectrum of cognitive decline. And when people who experience the mild cognitive decline and early signs, it often progresses to full-on

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Alzheimer's disease. And so because Alzheimer's disease is such an incredible concern in the United States in terms of cost socially and financially, anything that can slow the decline of cognitive function might wind up reducing this very devastating end result or slowing its progression. So I thought it was interesting to put in something about Alzheimer's disease to give the context in which this particular problem of mild cognitive decline is -- is important. It's just to fill out the context.

Q. And would that be the same reason why you included paragraph 24 on dementia?

A. Yes.

Q. And are you offering any opinions related to the efficacy of Prevagen and dementia?

A. No.

Q. How about are you referring any opinions related to the efficacy of Prevagen and Alzheimer's disease?

A. No, I'm not. I -- I'm offering opinions on the efficacy of Prevagen for mild cognitive dysfunction and the -- you know, a mild -- the milder level of decline. Dementia --

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Q. When you say --

A. Dementia is a further deterioration, and then Alzheimer's disease is one cause of dementia, but then there are other causes as well.

Q. When you say "mild cognitive dysfunction," is that the same thing as mild cognitive impairment --

A. Yes.

Q. -- that you discuss in paragraph 23?

A. Yes.

Q. So you are offering opinions in your report related to Prevagen and mild cognitive impairment?

A. Yes. I think that -- you know, it may -- it may be difficult to -- to form a red line between the normal cognitive decline of aging and mild cognitive impairment. The point is that -- that the question is will Prevagen help slow or reduce this trajectory.

Q. So are you offering opinions that Prevagen slows the progression of mild cognitive impairment?

MS. METZINGER: Objection to form.

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THE WITNESS: I think that I wouldn't make the claim. I wouldn't necessarily support a claim related to mild cognitive impairment because that would be a disease claim. So I used evidence on mild cognitive impairment to support the idea that Prevagen has a beneficial effect on cognitive decline. But I wouldn't support a claim for preventing mild cognitive impairment or Alzheimer's disease or dementia because those are disease claims not permitted under the guidance.

BY MR. WONE:

Q. Which guidance are you referring to?

A. FTC guidance, FDA guidance related to claims that are permitted. This is a structure function claim, not a disease claim.

Q. Earlier when we were talking about the Madison Memory Study, I believe you mentioned that there would be legitimate reasons to include people who scored a 3 or above on the AD8. Do you remember that?

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MS. METZINGER: Objection to form.

THE WITNESS: I believe that I said there that investigators might have a reason to recruit those folks into the study.

BY MR. WONE:

Q. And what would be some of those reasons?

A. Well, one reason for over-recruitment is to -- to account for dropouts. That could be 20 or 25 percent extra that you recruit because you want to have a final number of a hundred, so you might have to recruit 25 percent extra.

It's possible, and I don't know this because I haven't spoken with the researchers, so I don't know, but I could imagine that are situations where, when a clinical trial is being done, it's very expensive and very -- as I said, very time consuming, that with thinking towards the future, that an investigator might say, "Well, let's just kind of do the study on -- on everybody because maybe in the future, if it turns out we have people who have more serious

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cognitive decline, we'll want to look at those results." But for now, those -- that -- that -- those data are just going to be sitting because it's not our primary concern.

So I could imagine doing that as a scientist, trying to make the most of the resources that I have. I could imagine doing that.

Q. And in connection the Madison Memory Study, did you ever look at any data for participants who scored 3 and above on the AD8?

A. I -- I believe that might have been in one of the papers. I -- I guess I'm not sure -- I'm not sure right now if I did. I guess in the Advances paper they have data on AD8 2-5. So they do those show those data in that paper.

Q. Is it your understanding that the Advances paper was written before the data set was -- before the errors in the data set were identified?

A. Yes.

Q. And so you don't know whether the data that's presented in the Exhibit MK4 is accurate or not?

MS. METZINGER: Objection to

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form.

MR. WONE: I'll rephrase.

BY MR. WONE:

Q. Do you know whether the data depicted in Exhibit MK4 was accurate?

MS. METZINGER: Objection to form.

THE WITNESS: I don't know. You know, once I found out that there were errors, then I focused my attention on the corrected data and the results that were -- that were generated by the corrected data. So I don't know if that first paper is correct or not. I -- I didn't focus most of my attention on that.

BY MR. WONE:

Q. So you don't know whether Exhibit MK4 has corrected data?

MS. METZINGER: Objection to form.

THE WITNESS: I've been told that the data was corrected after this paper was published, so my assumption is that this is the precorrected data.

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Whether the results differ, I don't know.

BY MR. WONE:

Q. Okay. If a study had been unblinded through an interim analysis and the principal investigator had access to the information as to -- the data including what groups people were assigned to, would you agree that the study would no longer be considered double-blinded?

MS. METZINGER: Objection. Are you talking about any study or the Madison Memory Study?

MR. WONE: Hypothetically.

MS. METZINGER: Objection to form.

THE WITNESS: Hypothetically if a study were unblinded and the researchers knew who was taking which and/or the participants knew who were taking -- who was taking what, it would no longer be a blinded study.

BY MR. WONE:

Q. I believe you testified earlier --

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A. Mr. Wone -- Mr. Wone --

Q. Yes?

A. -- if I could add something to that?

Q. Sure.

A. Just to sort of repeat something that I said before, the fact that it is not a blinded study does not mean that the results are useless. The results may still be accurate even if it is not a double-blind study.

Q. Are you distinguishing between a study that was -- that's not blinded from the outset versus a study that was double-blinded but in which -- for which the blinding was broken?

A. I'm not distinguishing, no, no. I'm -- I'm saying that a blinding of the study is a very, very high threshold that's set for drugs and is important to stick to for studies like drug trials. But in my experience and in my opinion, I don't think that the results of an unblinded study or a not blinded study are false results. I've -- as I said before, I've published numerous papers from studies I've done that were not blinded, and I stand behind those results fully.

Q. If a study was unblinded and the

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investigators knew which participants who were assigned to each of the groups, could the data -- could the data from that study be biased?

MS. METZINGER: Objection to form.

THE WITNESS: That really depends on who is made aware of the data. If it's the principal investigators who are not interacting with the participants, that may not have any effect at all. I would be more concerned if it was the study coordinator, the person who is, for example, giving the tests directly to the participants. If they -- if that person, that staff member knew who was in which group, I might be concerned about that.

But I wouldn't -- if -- if it's a principal investigator who, like me, is a number of levels away from the participants, my knowledge isn't going to have any effect on the results.

BY MR. WONE:

Q. Could it have an effect on how

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you interpret the data?

MS. METZINGER: Objection to form.

THE WITNESS: The concern I would have would not be with the interpretation of data because when -- when I have a data set as a principal investigator, when I'm working on a data set with a statistician, I -- it's all numbers. The data is de-identified in the data analysis. So I have no idea who any individual person is.

The concern I would have here is in the administration of the cognitive tests if the person who is administering the test knows which group that participant is in, their interpretation of the results might be affected by that. Theoretically, it could be. But I would not at all be concerned at the level of data analysis working with a data set.

BY MR. WONE:

Q. Would your opinion change if there wasn't a statistician analyzing the data and

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the investigators were doing the analysis themselves?

MS. METZINGER: Objection to form.

THE WITNESS: No, my opinion would not change.

BY MR. WONE:

Q. I think we also mentioned that it was your understanding that the Madison Memory Study was 90 days?

A. Yes.

Q. And what was the basis for your belief?

A. I think it's stated in the protocol that it's a 90-day study. And in the publication, it's -- the study is described as a 90-day study, so I think it's very clear. I'm looking at the protocol now, and study duration, 90 days. And it says the same thing in the manuscripts.

Q. Okay. In your expert report, Exhibit MK1, you discussed corrections, correct?

A. Can you --

MS. METZINGER: Objection to form.

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THE WITNESS: Can you tell me which paragraph that is, please?

BY MR. WONE:

Q. I'm looking at paragraph -- sorry. Looking at Section 8.

A. Is there a -- okay. Section 8, issues related to the use of Bonferroni. Yes.

Q. What is the correction in this context?

A. The correction in this context is a correction for multiple comparisons, the idea being that when you do many, many, many comparisons, that some of those will show a significant effect by chance because you're doing so many.

And so in some situations, statisticians view -- feel that it's important to basically reduce your p-value so that you make it more difficult to find a significant effect in order to correct for the fact that there might be some random effects that you see because of the number of tests that you've done. That's my understanding.

Q. And what are some situations where you feel a correction would be appropriate?

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A. I think that Bonferroni -- I would be -- I'm very, very reluctant to take a general stand on Bonferroni. I think that it really needs to be decided on individual cases. It's a very, very strict requirement and it's fairly controversial.

And in the same sense that a p-value is an arbitrary number, an arbitrary cutoff, Bonferroni decreases the false positives, but it can have a big increase in false negatives. So it can reduce your ability enormously to see a -- to see an effect.

So I'm sure that there are situations with clinical drug trials where there's the impact of a mistake on -- in the data analysis is so critically important that you want to avoid false positives at any -- you know, you want to avoid at all cost false positives.

So, for example, you know, if you have a drug that's going to cure cancer, you know, you don't want false positives because you don't want to approve this drug and you -- you want to make it hard to see an effect for yourself because you don't want it to be approved unless you are a thousand percent sure that it's going to

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work. In that situation, I can see that a correction would be appropriate to do.

The problem with Bonferroni, as I say in my report, and I think it's a significant problem, is that if you really believe in Bonferroni and you feel that it should be used in every situation, then what will happen is in most cases we will never, ever be able to find a significant result for anything because even with some of the most widely respected and publicized and published clinical studies or epidemiological studies, there may be many, many, many papers published.

So, for example, the AREDS trial, which is an eye health -- eye supplement trial, there are at least 30 or 40 or 50 papers that have been published. And when people report data in the beginning, they don't account for future papers. They don't account -- you know, if we were to go back, okay, and say now that the 50 papers have been published, let's redo the statistics knowing how many different -- different analyses we did, nothing would be significant. We'd find zero significance.

And so people -- people tend

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to -- researchers tend to break their studies down into pieces in part because it's digestible for the reader. You just don't want to publish papers where you have so much in there that it's overwhelming.

You need to have theme to your paper. So you might publish your lipid results in one paper and your hormone results in another paper, and then you might publish some other -- you don't account for all of the comparisons in every paper. You can't do it because you aren't -- you know, you don't know in advance.

And so really if you take this -- if you take the Bonferroni -- if you believe that it should be used in every situation, then I think you have a real problem with finding any significant results at all.

But as I said, in the case of a situation like a drug that is critically important for peoples lives, you want to make sure that you reduce the pos- -- false positive as much as possible and you don't care so much about the false negatives.

So there's -- you know, it really depends on the situation, in my opinion.

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And in this situation where we're talking about a dietary supplement, which has very little -- which has no adverse effects, which is something which may confer some benefit to some people, I'm not worried about the false positive rate. I just wouldn't be worried about it in this situation. And the FTC guidance on regulating -- you know, on advertising for dietary supplements specifically gives a lot of flexibility and suggests to me -- my interpretation of the guidance is that the kind of rigor that's applied to clinical trials is to -- to drugs is not necessary for dietary supplements.

And so while in a clinical trial of a -- of a drug that is potentially going to lengthen or save someone's life who has cancer, I might in that case say, no, I agree that Bonferroni should be used. But in this case, I think it's really overkill. It's -- it's way, way, way more than necessary.

Q. You mentioned one particular type of correction, Bonferroni correction.

A. Mm-hmm.

Q. Are there other types of corrections?

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A. There -- I believe that there are many types of corrections. And the one that I've used when I have used a correction has been Bonferroni, so that's the one that I'm the most familiar with, but they're all variations on the same theme. They're all versions of the same type of correction, which is basically reducing your p-value threshold to account for the number of comparisons that you're making.

Q. And in the example you just gave in your prior answer, you mentioned researchers will have different papers, for example, a lipid paper. And so in that lipid paper, would you use a correction to account for multiple comparisons?

MS. METZINGER: Objection to form.

THE WITNESS: It depends on the number of comparisons that I've done, and it depends on the statistician who I'm working with and what their view is because very well-respected, well-trained professional statisticians differ on this point. And so I take the advice often from the statistician with whom I'm working, and so it really

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would depend on the individual case. There are many statisticians, and I have worked with a number of statisticians, and I find that the statisticians who have the most experience with biological data, with human data, are much more flexible in interpreting statistical results because of the things that we talked about before.

BY MR. WONE:

Q. And you've mentioned you -- you've used Bonferroni in your own research, correct?

A. I believe that I have. I'd have to look at my papers to see where I might have used it, but I -- I probably have used some kind of multiple -- multiple comparison testing, multiple comparison correction. But not very often for the reasons that I said because it really reduces your ability to see a true effect.

Q. So I'm introducing what's been marked as Exhibit MK7.

A. Yep.

Q. Do you see that, Doctor?

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A. I do.

(Marked Exhibit MK7.)

BY MR. WONE:

Q. And it this one of your research papers, Doctor?

A. It is. It's a paper from 20 years ago, I see. And my students are on it who I'm very proud of. Alison is a full professor now, so, yes.

Q. If you could turn to page 227 of that, of Exhibit MK7. I'm referring to the page numbers that are depicted in the top right corner.

A. 227, yes. Yes.

Q. Do you see the data analysis section?

A. Yes.

Q. And the second paragraph of that section, do you see a mention of the Bonferroni correction?

A. Yes.

Q. And do you see that the Bonferroni correction was applied to p-values to adjust for multiple comparisons?

A. Yes.

Q. And what were the comparisons

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being made in this study in Exhibit MK7?

A. So we were looking at three different diets, and we were looking at LDL peak particle diameter, LDL -- and concentrations of triacylglycerol apo A-1, apo B, lipoprotein(a), total ADL and HDL cholesterol. So there were eight different endpoints and three different diets so that each of the diets was compared with each of the other diets.

Q. And why did you use the Bonferroni construction in this study?

A. I use the Bonferroni correction in this study because the statistician I was working with probably insisted that I use it because that was his belief, and so I agreed that we would use it. But if I had been working -- frankly, if I had been working with a different statistician, they might have said we don't need to.

But this is probably more comparisons than I often do in my studies, and so it was -- I accept this recommendation.

Q. And do you know whether the comparisons in this study were correlated?

A. Yeah, I think that some of them

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are. Yes, some of them are correlated. Not all of them.

Q. And did this study involve a dietary ingredient?

A. Yes. It involved soy -- soy protein intervention.

Q. And what were you studying in this article in relation to soy?

MS. METZINGER: Objection to form.

THE WITNESS: What's that? Excuse me? Can you ask --

BY MR. WONE:

Q. What were you studying in Exhibit MK7 in connection to soy?

A. Oh, we were looking at the effect of soy protein consumption on plasma lipids.

Q. Did the study involve any investigation of a disease?

A. No. No, it didn't. It -- we looked at lipid levels in the blood which relate to disease but are not a disease endpoint themselves.

Q. And did the study depicted in

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MK7 involve a drug?

A. No, it didn't. It involved a food or, you know, dietary substance.

Q. So I'd like to introduce what has been marked as Exhibit MK8.

(Marked Exhibit MK8.)

THE WITNESS: Okay.

BY MR. WONE:

Q. Do you see that, Doctor?

A. I do.

Q. And were you an author on this study in Exhibit MK8?

A. Yes.

Q. And what did this study in Exhibit MK8 involve?

A. This involved the evaluation of consumption of green tea, green tea extract with the bioactives in green tea, the effect on serum lipids in postmenopausal women.

Q. And green tea extract is a dietary ingredient?

A. Yes, it is.

Q. And the study depicted in Exhibit MK8 did not involve a disease, correct?

A. That's correct.

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Q. If you could turn to page 1673 in Exhibit MK8. And I'm referring to the page numbers on the top corners of the page.

A. Yes.

Q. In the right hand column, the last paragraph before the result section, do you see that, Doctor?

A. Yes.

Q. And do you see in the last sentence that the Bonferroni correction was used to adjust for multiple comparisons?

A. Yes.

Q. Why did you apply the Bonferroni correction in the study depicted in Exhibit MK8?

A. Again, I was working with a statistician whose name is Renwei Wang, and Jiam-Min Yuan, who are -- their experience is with enormous data sets. They're epidemiologists, and their experience is with huge data sets in which they look at every dietary substance that the person consumes in relation to cancer risk. They may do hundreds and hundreds and hundreds of comparisons in their papers.

So my opinion is that this is a standard practice for them, and they have -- I

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don't believe they had ever done a clinical trial before this. They were using statistical methods that were -- that are probably more conservative than necessary, but I accepted it because I -- you know, I -- I relied on them and I didn't argue with them. They also were difficult to argue with as far as people. And so I accepted that correction. I'm not sure that it was necessary for this particular paper.

In addition, this was one of those studies that was not in the original protocol. So the original protocol did not have lipids in it. There wasn't part -- we added it on because during the study, we realized that there is some evidence that green tea may be associated with beneficial effect on blood lipids, and so we decided to add this on. It didn't change our statistics. We did comment that it was an ancillary study so that this was -- and we did a subgroup analysis as well, I recall. We looked at hypercholesterolemic women as well as normal cholesterolemic women. I believe we separated them out. Hang on one second.

Well, we looked at the -- in table 5 on page 1679, you can see that we looked

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at blood lipids stratified by baseline BMI because we thought that could be a factor that is important to take into effect.

On the next table, 6, we actually also separated out those who used statin from those who didn't because we thought that is probably an important factor. It wasn't something we thought about in the beginning of the study because we weren't planning on looking at lipids, so statins weren't something that we were thinking about.

So this is something that we added on and that we did do subgroup analysis because ultimately -- my philosophy is -- and a very, very strict statistician might disagree with me, but I'm more concerned with getting the truth and getting the result that's real and important that I am about whether or not a particular test which may or may not be appropriate for this data set is used.

So, for example, looking at people who are taking statins versus people who aren't seemed like a really important way to look at the data.

Q. And you noted in the study

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report in Exhibit MK8 that this was an ancillary study?

A. Yes. But it didn't affect how we did the statistics, but we did note that so that the reader could see.

Q. And when you applied the Bonferroni correction to the comparisons, do you know whether the comparisons in the study in Exhibit MK8 were correlated?

MS. METZINGER: Objection to form.

THE WITNESS: I don't -- I don't remember. I'm -- I'm sorry, I don't remember that. I'd have to --

BY MR. WONE:

Q. What were the --

A. -- study the paper a little more.

Q. What were the comparisons that were being made in -- in Exhibit MK8?

A. Okay. So we were looking at the effect of green tea extract on total cholesterol, HDL cholesterol, and triglycerides. And we had the placebo group and we had the treatment group, and we also stratified by a genotype, a genetic

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polymorphism in the COMT gene which we thought might affect metabolism of catechins and, therefore, the biological effect of catechins.

Q. And do you know whether triglycerides and HDL are correlated?

A. You know, right off the hat -- the bat, I -- I don't recall. I think we probably looked for that in here. We probably did some tests to determine whether or not they're correlated because that would influence the statistical -- the type of statistical test that's used. And I don't recall. I'd have to study this a little bit.

Q. You can look through the article if you'd like.

A. Okay. Thank you.

I'm sorry. I don't see it. I don't see that we looked for it. Unless you can point me to something, I don't see that we looked at correlation among those -- among those endpoints.

Q. Okay. When you worked --

A. But I would -- I will tell you that this study reflects one of the weaknesses or one of the limitations of clinical trials, which

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is that despite the fact that we recruited a thousand women and we randomized them really perfectly, there was a difference in baseline lipids between the two groups. It's just -- and that's happened to me in other studies too. It's just bad luck. And that happens. And it makes your -- you know, the data analysis a little bit more difficult. And it's very disappointing when that happens, but that's something you find out at the end of the study.

Q. Okay. And when you're working on an RCT, you rely on the statistician to decide whether a correction is appropriate?

MS. METZINGER: Objection to form. Mischaracterizes the witness' testimony.

THE WITNESS: I wouldn't say I rely on a statistician. I rely on my relationship with them and conversations with them. So I take their advice very, very seriously just as when I'm a -- when I'm a collaborator on a study where I'm the only person who has a Ph.D. in nutrition, I hope that they take my

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advice when I point out things. But that doesn't mean they shouldn't be doing the study or, you know, they -- they -- we don't -- we -- these days we work in teams, and people have different areas of expertise, so it's extremely common to have -- you know, to have someone -- to have a statistician or a nutritionist who interacts with the others and the decisions are made as a group collectively.

BY MR. WONE:

Q. We can go back to your expert report, Exhibit MK1.

A. Yes.

Q. And go to paragraph 47, please.

A. Okay.

Q. In paragraph 47, you mention the word "correlated." Could you explain what you meant by "correlated" in the context of paragraph 47?

A. What I meant is that they are not independent of each other. They are either affected by the same underlying cause or they

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are -- they move in parallel to each other so that you would expect that an effect on one would probably be similar to an effect on the other. That's what I mean by "correlated."

Q. Do you know whether all aspects of cognitive function are correlated?

MS. METZINGER: Objection to form.

THE WITNESS: I don't know in the statistical sense whether they're correlated, but I know in the common sense that they're correlated because the factors, if you -- if you look into detail on each of these different factors and -- and I did do that for this exact reason, you can see that many of the same things contribute to each of these endpoints. So --

BY MR. WONE:

Q. How --

A. Yeah.

Q. Go on. I didn't mean to cut you off.

A. So that -- so that -- you know, if attention -- as we said before, I think we

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talked about this before, you know, in order to learn, you have to have memory. You have to have a good memory to learn. You have to be able to pay attention. So there's all -- there's a -- every -- I think that even the folks in this field agree that there is overlap among these. That would result in them being highly correlated. They're not independent if there's overlap.

Q. So you described I think what you meant by common sense correlation, but you distinguished it from statistical correlation. What is the difference?

A. The difference is that I haven't seen the statistical data to show that these -- I -- I didn't pay a lot of attention when I was writing this up to the statistical data showing that these endpoints are statistically correlated with each other because there are methods of statistical analysis that can determine correlation independence. And I don't recall seeing those kinds of data that actually statically prove the correlation. But if something -- if a measurement includes pieces of another measurement, it just makes sense that they're correlated, they're not independent.

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Q. And how do you know whether -- how do you know the level of correlation between two things that are not independent?

MS. METZINGER: Objection to form.

THE WITNESS: That would require a statistical test to be able to see the level of correlation. But, you know -- for example, you know, just out of kind of real life, I think that I can say pretty conclusively that it's easier for tall people to reach my upper cabinets than it is for short people. I don't need to do a statistical test to prove that, you know. I just know that. So that's where I say common sense has to come into this, that if you're a statistician, you're going to go, oh, my, do you have enough participants and have you done the right tests. There are some things that are fairly obvious.

BY MR. WONE:

Q. So if I'm understanding you

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right, you believe that memory and executive function are correlated, correct?

A. Memory and executive function, I would say probably. But certainly memory and attention are correlated. I'm certain of that. And sometimes people talk about concentration, and concentration and attention seem to be very, very overlapping concepts.

So executive function is kind of unique, so I would have to think about that a little bit, whether executive function would be -- would be related but -- to some of these others.

But there's a concept of working memory. And they often talk about working memory versus executive function. They're very, very overlapping. You know, executive function is the ability to manage many things in your brain at the same time. And working memory is very similar. It's the ability to manipulate thoughts and ideas and concepts. So they're very, very similar ideas.

Q. And do you know the level of correlation between memory and attention?

A. I don't know the level of correlation, no.

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Q. Do you know the level of correlation between working memory and executive function?

A. I do not.

MR. WONE: Can we go off the record for a moment?

THE VIDEOGRAPHER: We are going off the record at 1:51 P.M.

(Off the record from 1:51 until 1:52.)

THE VIDEOGRAPHER: We are going back on the record at 1:52 P.M.

BY MR. WONE:

Q. So in paragraph -- I'm sorry, on page 11 of your expert report --

A. Yes.

Q. -- Exhibit MK1, you mentioned that the -- you believed the data from the Madison Memory Study should be analyzed as a whole, correct?

A. Yeah, it should be looked at as a whole, yes.

Q. And what did you mean by that?

A. What I mean is that in the context of my report that the statistical

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comparisons are important, but it's also important to look at trends. And as I said before, I think that trends are extremely important. And many of my colleagues who do human studies with dietary substances agree that trends are important to report because we often don't have the statistical power to -- you know, we don't -- we don't have, you know, the ability to recruit a thousand people or 500 people. And so it's very, very difficult also with all of the factors that influence and cause variability between people. It's very difficult for us to get statistical -- to statistically significant results. Everything is stacked against us. There's an enormous amount of variability that humans have that we don't have with animal experiments. And because we don't even know what some of the factors are contributing to variability, we can't control for them.

So because of that, I think it's very important to not just very narrowly and very strictly look at the p-values, but also to look at trends. And I don't know if you have any of my papers pulled up, but I have many papers where I talk about trends and I report them. So that's

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what I meant by looking at the data as a whole.

Look at the statistical analysis, yes, it's important. No question about it. But it's also important to see that the trends that are observed are unlikely to occur randomly.

Q. Let's talk about the Madison Memory Study. Did you look at the entire population of the Madison Memory Study?

MS. METZINGER: Objection to form.

MR. WONE: I'll correct it.

BY MR. WONE:

Q. Did you analyze the data for the entire population of the Madison Memory Study?

MS. METZINGER: Objection to form.

THE WITNESS: I don't believe that I did. I focused on the manuscript, so I don't -- I don't -- that they reported on that.

BY MR. WONE:

Q. Now, when you look at the entire population in the Madison Memory Study, was there statistically significant results between group on

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any of the measures?
A. Can you point me to the paper where that would be and I'll -- I'll look at it more closely?
MS. METZINGER: I'll just note my objection to the form of that question as well.
BY MR. WONE:
Q. So if you go to Exhibit MK3.
A. MK3, mm-hmm.
Q. And turn to page 5. And I'm referring to the page numbers on the bottom corners of the document.
A. Yep.
Q. First line of the result section.
A. Okay. Mm-hmm. I see that.
Q. Do you understand that to --
A. They did do -- they did do an analysis of the entire population.
Q. And do you agree that there were no statistically significant results for the entire population?
MS. METZINGER: Objection to form.

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THE WITNESS: I don't see the data. I believe their sentence. I believe their statement, but I don't see the data, so I couldn't comment on it.
BY MR. WONE:
Q. You don't have any reason to disagree with what's written in that sentence --
A. That's correct. That's correct.
Q. Okay. If we could go back to your expert reports, Exhibit MK1. If you could go to paragraph 33.
A. Okay.
Q. Kind of in the middle of the paragraph where you're discussing the results of the AD8 0-2 group, you use the phrase "significantly more."
Do you see that?
A. Yes.
Q. And when you said "significantly more," what kind of significance did you mean?
A. I meant statistically significantly more.
Q. Do you know whether the improvement was clinically significant?

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A. I don't know if the improvement is clinically significant, but I do believe that the effect size is -- is a medium to high effect size when you look at the effect size. But -- but I do not know whether or not -- what the level of clinical significance of these differences are.
Q. Could a medium to high effect size still be clinically -- not clinically significant?
MS. METZINGER: Objection to form.
THE WITNESS: That's a hard question to ask, Mr. Wone -- to answer, Mr. Wone. I think it depends on the situation.
BY MR. WONE:
Q. I'm talking about the situation specifically in the Madison Memory Study.
A. It is possible. It is possible that statically significant results are not clinically significant.
Q. Okay. Further down in paragraph 33, last full sentence starting with within the AD8 0-1 group --
A. Yes.

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Q. -- you again use the phrase "significantly more."
Do you see that?
A. Yes.
Q. And were you referring to statistical significance in this --
A. Yes.
Q. -- sentence?
A. Yes.
Q. Do you know whether the improvement you mentioned in this sentence in paragraph -- the last sentence of paragraph 33 was clinically significant?
A. I can't comment on that.
Q. Do you know whether any of the measures in the AD8 0-2 group that were statistically significant measured memory?
A. Okay. So it was the -- so the three tests that were statically significant were tests that measured executive function, attention, and visual learning. Visual learning certainly requires memory. Right? You can't learn something unless you can remember it. It requires memory. So memory is connected with visual learning.

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In addition, executive function, your ability to -- to organize your thoughts and -- requires that you can remember things. Otherwise, you cannot organize them.

So the statistically significant ones were not tests that focused on memory as a primary outcome, but they certainly require good memory in order to be good on those tests.

And the -- there are a couple of other tests that do specifically point -- are specifically said to test memory itself, which are the delayed recall tests, and -- and those tests, I believe, showed a trend towards being effective.

Q. Did any of the measures in the AD8 0-2 group that focus on memory specifically have statically significant results?

A. No.

MS. METZINGER: Objection to form.

BY MR. WONE:

Q. So even though none of the measures for the 0-8 group -- 0 -- sorry.

Even though none of the measures for the 0-2 group that had memory as a specific -- as a specific outcome was statically significant,

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you would still conclude that Prevagen has improved memory?

A. Yes.

MS. METZINGER: Objection to form.

THE WITNESS: Yes, I would. And the -- and the reason, Mr. Wone, is a couple of things. One is that there's a reason why a battery of tests is being done. There's a reason why they don't just do one test because they need to capture as many aspects of memory and cognitive function as possible. So they do these battery of tests. And, in fact, some of them supposedly focus on the same thing. So there are a few that focus on memory.

But that's why you do a battery of tests, because no one test in itself is going to tell you whether or not -- whether or not memory is affected. You have to look at all of them. That's why they do batteries of tests.

You know, you will never see something related to brain function,

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a -- a test given to humans related to brain function. It's very rare that you'd ever see one. All of the different tests that are -- that are used and have been validated and are used in research studies have multiple aspects of them, whether it's a subjecting survey that's given or tests like this. You have to give a battery to capture the result because any -- the result of any one is not nearly as meaningful as the overall result of all of them.

And because three out of nine showed statistically significant effects in the direction of a benefit for apoaequorin and then five additional tests showed a trend in the direction of benefit, my interpretation of that is that that is extremely unlikely to happen by chance, that if everything were random, you'd expect to see not only five tests that show no results, but you'd accept -- you'd expect to see as many tests showing the

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placebo is better than apoaequorin as you see showing that apoaequorin is better than the placebo, and you just don't in these data. The data as a whole then you look at it is pointing in the direction of a benefit statically and also via trends.

BY MR. WONE:

Q. I'm sorry. What was the last word you said? Via?

A. Statically and also by looking at trends. Looking at the statistics and the trends together for all nine of these tests, to me the conclusion I reach is that there is a benefit.

Q. You've mentioned trends, so why don't we return to a page in your report where we discuss that further. If you could turn to page 11, paragraph 50, please.

A. Yes.

Q. And in this section, you state that conclusions should be drawn logically?

A. Mm-hmm.

Q. What did you mean by that?

A. Well, by logic, what I mean is what I was talking about before, that there's a

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certain amount of common sense and logic that needs to be applied in the context of statistical analysis.

It's very easy for statisticians to get caught up with numbers and to forget the bigger picture of what they're looking at, and all they care about is the p-value and the corrections and that's where they stop. And they may not have any knowledge of the biology at all. They may completely not know anything about biology. All they know is mathematics and -- and that's where their knowledge ends.

What I mean by logic or common sense is that, as I said -- and this could even potentially be a statistical point, is that when you look at table 1, which is on the next page, and you see the nine tests and you see that -- that three of them show a statistical benefit in the direction of effectiveness, one of them shows exactly the same effect, so there's no -- no difference. And the other five show the direction of the difference is in direction of benefit of apoaequorin.

And what I mean by logic is that is very unlikely to have happened by chance, that

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if you were expecting the effects to be totally random, that if you see three statically significant results in the direction of benefit of apoaequorin, you ought to see three statistically significant effects in the direction of benefit of the placebo. That would be random. And the trends should also be showing trends in both directions. That would be random.

If what you see is statistical significance with a few of these and most of the others show the direction of a benefit, my interpretation of this, and this is using my logic, not using a statistical analysis, it's using other parts of my brain to understand this, is that the totality of the data here point very clearly in the direction of a benefit.

Q. Are there standards that experts in your field use to draw conclusions logically?

MS. METZINGER: Objection to form.

MR. de LEEUW: Objection to form.

THE WITNESS: No, there aren't and standards for logic. And I would say that -- but I would say that many,

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many of my colleagues would agree with me about this. Many colleagues who work in nutrition, who work in the fields -- some field related to dietary supplements who would look at this would agree that trends are very, very important, people who do human experimentation and understand the variability. Particularly, researchers who are looking at very, very low risk substances, the trends would be extremely important.

So I don't think that there is a standard. But, in my view, the fact that there isn't a standard doesn't mean that it's not right.

BY MR. WONE:

Q. And so it's possible that another expert in your field could draw a different conclusion even though both of you are looking at something logically?

MS. METZINGER: Objection to form.

THE WITNESS: Anything is possible.

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BY MR. WONE:

Q. Okay. In paragraph 50, you also use the phrase, and we've -- you've used it earlier today, "nonsignificant trend towards efficacy."

A. Yes.

Q. Do you see that?

A. Yes.

Q. And when does something trend towards efficacy?

A. The trend reflects the direction of the absolute changes. And, you know, I will say that I know that one of the -- one of the statistical experts, FTC experts, said it's not statically significant, end of story, you don't even talk about it. And I disagree with that very strongly.

I -- I certainly feel, and I teach my students this all the time because they make the mistake of saying simply this -- the treatment differs from the placebo because the absolute number is different without clarifying that they're not -- they are actually not statically significant. So that's true, in a statistical sense they're not different. But --

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and so you should never ever say that they're just flat-out that they're different if it's only the absolute differences.

But you certainly can say, and it's perfectly permissible to say, there is a difference, but it's not statistically significant especially when in the context of what we're talking about here, which is a number that are all trending in the same direction. That's when trends really interest me.

If it's just a one-off thing that is a trend, I probably wouldn't comment on it. If one of them was going in the direction of benefit, I wouldn't have valued that very much. But when almost all of them do, to me, that's where I say we got to look at this and take this -- take this, you know, as important -- an important result.

Q. And would even a small amount of improvement in the direct -- sorry.

Would even a small increase towards the direction of improvement mean that something trend towards efficacy?

MS. METZINGER: Objection to form.

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THE WITNESS: Yes, I think that it does in the context of having nine tests here. So you have to keep remembering context that we're talking about. You know, if there was one small change in the direction of efficacy in -- in a large group, I would not say that that's important. But the fact that five out of nine of these or -- or let's say there were three significant results and five out of six of the other results go in the direction of efficacy, as I said before, I hate to keep repeating myself, it is unlikely to be random, a random effect.

So in the context of all of these tests being done, I would make that statement. But I would not necessarily make that statement about one result. I wouldn't look at one result necessarily and say it's trending in a certain direction. But because it's a group of results, then it becomes more interesting.

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BY MR. WONE:

Q. You used the expression earlier that something cannot -- that it can't be explained by chance. So I'd like to I guess understand, when you say it can't be explained by chance, what do you mean?

A. What I -- what I said was that it's very unlikely to be explained by chance. And what I mean by that is if you have -- if you have eight tests that you're giving, that randomness, if the effects are entirely random, you would not expect to see any kind of pattern. You'd expect to see results going in every direction. And that would -- that is what randomness means. It means there is equal probability of the result going in one direction as there is of the result going in the other direction. And so because of that, you should see the results going in both directions. But -- and that's what I mean by -- by unlikely to be explained by chance.

Q. And so if you don't see the results going in both directions, you believe it's unlikely, but it's not impossible that it's -- it could still be related to chance, correct?

MS. METZINGER: Objection to form.

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THE WITNESS: Well, Mr. Wone, it could be related -- it could be a result of chance in the same way that even if you get a p-value of .05, it's possible that that really was a result of chance too. As I said, anything is possible when you're talking in the -- in the world of hypotheticals. But it's very, very unlikely, which I think is a more relevant -- a more relevant approach to this than -- than using whether it's possible or not.

BY MR. WONE:

Q. And in the -- in the Madison Memory Study when you describe measures as trending towards efficacy, do you know whether those improvements were clinically significant?

A. I do not. I cannot -- I cannot answer regarding clinical significance.

Q. Well, let's look at one of your tables. If you could turn to page 12, table 1. Do you see that, Doctor?

A. Yes, I do.

And I apologize if you can hear

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the lawn mower in the background. They'll be gone in a couple of minutes.

Q. I cannot, so --

A. Okay. Good.

Q. -- we're fine.

And so in the second column, when you say "Direction of Improvement, Increase" or "Decrease," what did you -- how did you decide whether to put increase or decrease?

A. The direction of improvement in this particular -- in this particular column refers to the direction -- some of these tests, if you -- if the -- if the number goes down, it's a good thing. And others of the tests, if the number goes up, it's a good thing. So that's what this is saying, that with the ISL and the ISRL, if the numbers increase, that shows improvement. With the GML and the GMR, if the numbers decrease, that shows improvement. So that's what that column is referring to.

Q. Okay.

A. I'm sorry if it wasn't clear.

Q. And so for the last two, ONB, a decrease means that if the number went down, that would be an improvement?

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A. That's correct.

Q. So I'd like to introduce what's been marked as Exhibit MK9.

(Marked Exhibit MK9.)

THE WITNESS: Okay.

BY MR. WONE:

Q. Do you see that, Doctor?

A. Yes.

Q. Okay. And just to, I guess, go back. When you said in your report in table 1, ONB, what measure was ONB?

A. They -- I think the one -- the one card back. Is that the one that it is?

Q. Okay. And do you know what TWOB was?

A. The two card back.

Q. And if you could go to -- back to Exhibit MK9 and turn to page 4.

A. Okay.

Q. Do you see the -- under the task name "One Back"?

A. Yes.

Q. And do you see the fourth column under description?

A. Yes.

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Q. And what does under description -- under description, what does the document say a higher score means on the One Back?

A. Higher score is better performance.

Q. Going back to your report in Exhibit MK1, what did you write in the direction of improvement for the One Back?

A. I wrote decrease.

Q. And so does the document I've shown you in Exhibit MK9 change your opinion about whether a decrease or increase is the direction of improvement?

MS. METZINGER: Objection to form.

THE WITNESS: Hang on one second.

It looks like that's correct. It looks like that there's an error somewhere because this does not agree with what I had in my report. And I did not have access to this Cogstate document when I was writing my report. I've not seen this Cogstate document before. And so I was using other

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documents in order to -- to determine which direction the benefit or effectiveness would be shown. But it looks as though you're correct, that the One Back test -- in the One Back test, the Cogstate document says that a higher score is better performance.

BY MR. WONE:

Q. Okay.

A. And in my document, I wrote that a lower score is better -- is better performance. So there does seem to be some kind of error between the two.

Q. And so when you report in table 1, the direction of improvement for the One Back should be increase, not decrease?

A. Yeah, if the Cogstate document is correct, then you're right, it should be increase rather than decrease.

I would want to see the -- not just the Cogstate document -- which, of course, is probably correct. I don't doubt that. But I would want to look at some of the other sources I had to try to see why I put decrease and see if it's possible that there's some other kind of

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error.
But assuming that the Cogstate document is correct, then you're right, that's -- that's a mistake.
Q. And assuming that the Cogstate document is correct, does it also mean that in table 1 the -- when you change increase -- decrease to increase, that the placebo outperformed the treatment group on the One Back?
A. That's correct.
MS. METZINGER: Objection to form.
BY MR. WONE:
Q. And is it also correct to say that instead of "effective" in the last column on the right, it should say "placebo better"?
A. Yes.
MS. METZINGER: Objection to form.
BY MR. WONE:
Q. I'd like to go back to Exhibit MK9. If you could go back to page 4 and look at the task for Two Back. Do you see that, Doctor?
A. I do.

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Q. And do you see what the description column says for the Two Back regarding higher score?
A. Yes. Higher score, better performance.
Q. And what did you say -- Two Back in table 1 of your report in Exhibit MK1?
MS. METZINGER: Eric, your audio cut out for that question.
MR. WONE: Sure.
BY MR. WONE:
Q. What did you say the direction of improvement should be in table 1 of your expert report --
A. The same thing as --
Q. -- for the Two Back?
A. -- the other, decrease. And it looks as though it should actually be increase if the Cogstate report is correct.
Q. And if the direction improvement for the Two Back should be increase, does that mean that the placebo group outperformed the treatment group?
MS. METZINGER: Objection to form.

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THE WITNESS: I would say that the trend would be in that direction.
BY MR. WONE:
Q. And so the trend should say, instead of "effective" for the Two Back in table 1, it should say "placebo better," correct?
A. Yes.
MS. METZINGER: Objection to form.
BY MR. WONE:
Q. And going on to table 2 of your expert report, which is on page 13, should the direction of improvement for the One Back in table 2 also say "increase"?
MS. METZINGER: Objection to form.
THE WITNESS: Yes.
BY MR. WONE:
Q. And with that change to say "increase," did the placebo group outperform the treatment group on the One Back measure in table 2?
A. Yes.
MS. METZINGER: Objection to form.

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BY MR. WONE:
Q. And so instead of "effective," it should say "placebo better" in the trend column for the One Back, correct?
A. Correct.
MS. METZINGER: Objection to form.
BY MR. WONE:
Q. And how about the Two Back in table 2? Instead of "decrease," should it also say "increase"?
MS. METZINGER: Objection to --
THE WITNESS: Yes.
MS. METZINGER: -- form.
BY MR. WONE:
Q. What was your answer, Doctor?
A. Yes.
Q. And with that change to increase, did the placebo group outperform the treatment group on the Two Back in table 2?
MS. METZINGER: Objection to form.
THE WITNESS: Yes.
BY MR. WONE:
Q. And should the trend for the Two

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Back in table 2 say "placebo better" instead of "effective"?
A. Yes.
MS. METZINGER: Objection to form.
BY MR. WONE:
Q. So with these changes to table 2, how many measures trend towards placebo?
MS. METZINGER: Objection to form.
THE WITNESS: In table 2, which is the 0-1 group, which is not the exact group of interest, then what we find is that three of the endpoints are -- show statically significant effectiveness. And of the other six, three of them, the trend -- I would -- I would say that the trends are not -- don't -- are not helpful in -- because they cancel each other out.
So there were -- in the trends, there were three that go in the direction of apoaequorin effectiveness and there are three that go in the direction of the placebo being better.

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But that doesn't take away from the fact that the only statistically significant effects that were seen are three in the direction of -- of apoaequorin.
BY MR. WONE:
Q. Wouldn't there be four measures that are placebo better?
A. Oh, I'm --
Q. One --
A. -- sorry.
Q. -- Back --
A. Right.
Q. One Back, Two Back --
A. Ah --
Q. -- ISLR --
A. -- yes.
Q. -- and the --
A. Yes.
Q. -- IDN?
A. Yes, that's right. And the --
MS. METZINGER: Objection to form.
Dr. Kurzer, just give me a moment to state my objection before

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you --
THE WITNESS: I'm sorry.
MS. METZINGER: Thank you. You can go ahead.
BY MR. WONE:
Q. What was your response to my question, Doctor?
A. That's correct, in the 0-1 group, if what you're saying is correct, that the One Back and Two Back should be increased in the direction of improvement, then there are three tests that show statically significant benefit of apoaequorin. And of the six other tests that do not show statistical significance, two are trending in the direction of effectiveness of apoaequorin and four are trending in the direction of the placebo being better.
Q. So if -- if five measures overall trend toward treatment and four measures trend towards placebo, would you agree that that is close to what you would expect for a random effect?
MS. METZINGER: Objection to form and mischaracterizes the witness' testimony.

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THE WITNESS: In this case, with this table, I think the fact that we find three to be statically significant in the direction of efficacy and we find none to be statically significant in the direction of the placebo being better, it still provides evidence providing towards efficacy of -- of apoaequorin.
And if you look at the A through 2 group on the previous table, table 1, I think it's even more the -- what I just said is even more apparent because there are only what -- in table 1, when we look at the 0-2, which in my view, my interpretation of the methods and the protocol is that this is the group of interest, that there are three tests that show statistical significance in the direction of effectiveness, that show statistically significant effectiveness, that there's one that shows no difference, that there are two that show a trend towards the placebo being better, and there are

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then three that show a trend towards the apoaequorin being better.
So this table 1 is more relevant than table 2, although I think they both provide evidence that apoaequorin is effective. I think table 1 is more relevant and the data are a little bit stronger.
BY MR. WONE:
Q. Are participants in the AD8 0-1 group healthy older adults?
A. Yes, in my opinion they are.
Q. And it's your opinion that Prevagen is intended for healthier older adults?
A. Yes.
MS. METZINGER: Objection to form.
BY MR. WONE:
Q. If we could go to paragraph 52 of your report --
A. Mm-hmm.
Q. -- Exhibit MK1.
A. Yes, I'm here.
Q. In your second to last sentence, you say that the -- starting with "As is true," do

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you see that sentence?
A. Yes, I do.
Q. You use the phrase "strongly suggestive of a benefit of treatment."
What did you mean by "strongly suggestive"?
A. What I mean is that the data suggests a benefit of treatment. And the word "strongly" is meant to sort of emphasize that a little bit.
Q. And given the changes we've discussed, is it still your opinion that the data is strongly suggestive of a benefit of treatment?
MS. METZINGER: Objection.
THE WITNESS: I would probably --
MS. METZINGER: Go ahead. Thank you.
THE WITNESS: I would probably take out the word "strongly" and I would say it is suggestive of a benefit. I still believe that table 1 -- that table 2, excuse me, is suggestive of a benefit, although not as strongly as table 1.

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BY MR. WONE:
Q. And when something is suggestive of a benefit, does that mean it's not proven?
MS. METZINGER: Objection to form.
THE WITNESS: To me, the word "proven" is not a very useful word because in science, as you well know with -- there is a -- a spectrum of proof, and you have to decide what your threshold is for accepting that evidence. It's very hard to say that anything is proven in the sense that -- you know, that absolutely a hundred percent. It's really what is the threshold of evidence. And in this case, I would say that the threshold is met for it to be -- for there to be a benefit from apoaequorin.
BY MR. WONE:
Q. So if I'm understanding you correctly, you believe the threshold for showing a benefit of apoaequorin is met when the data is suggestive?
MS. METZINGER: Objection to

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form.
THE WITNESS: I think that the word "suggestive," you're interpreting it as meaning -- you're interpreting it a little bit differently than me. I'm using the word "suggestive" because we haven't proven statistical significance for all of the endpoints, and so I'm using that word to soften my conclusion a little bit. But I could have written it differently and said it is suggestive of a benefit of treatment, but I wanted to acknowledge that there were some results that did not statically show benefit.
BY MR. WONE:
Q. And you also don't know whether the benefits that you saw were clinically significant?
A. That's correct.
MS. METZINGER: Objection. Asked and answered.
MR. WONE: Can we go off the record for a moment?
MS. METZINGER: Sure.

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THE VIDEOGRAPHER: We are going off the record at 2:36 P.M.
(Off the record from 2:36 until 3:07.)
THE VIDEOGRAPHER: We are going back on the record at 3:07 P.M.
BY MR. WONE:
Q. Dr. Kurzer, if you could go back to your expert report, Exhibit MK1, please, and turn to paragraph 47.
A. Okay.
Q. In that paragraph, do you see an article by Eichstaedt cited?
A. Yes.
Q. Hold on a second. Sorry. Okay. I'm introducing what has been mark as Exhibit MK10.
(Marked Exhibit MK10.)
BY MR. WONE:
Q. Do you see that, Dr. Kurzer?
A. I do.
Q. And is this the Eichstaedt article that you cited in your expert report?
A. I assume that it is because you're telling me so. So, you know, it is --

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Eichstaedt is the first author, so I assume that that's correct, yes.
Q. In this article, Eichstaedt discusses an alternative to Bonferroni --
A. Mm-hmm.
Q. -- correct?
A. Yes.
Q. And what was the alternative that Eichstaedt mentioned?
A. It's a different type of -- of correction called "The Holm's sequential Bonferroni procedure."
Q. And do you agree that Eichstaedt believes that Holm is better because it protects against heightened type 1 error without increasing -- unnecessarily increasing type 2 error?
MS. METZINGER: Objection to form.
THE WITNESS: I believe that that's what they are saying.
BY MR. WONE:
Q. And was Eichstaedt recommending use of the Holm correction in -- in neuropsychological studies?

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A. They're saying that it may be a better test than the Bonferroni.
Q. Do you believe that Holm would be an appropriate correction to apply in the Madison Memory Study?
A. I can't answer that from just seeing one paper making this suggestion. My reason for citing this was just to add to the literature showing that there isn't necessarily a consensus among statisticians. But I haven't seen the Holm's sequential Bonferroni applied to these data and so I can't comment on if it would be appropriate or not.
It may be that it's -- that it's -- that it turns out to be overly strict just as Bonferroni is, although they say that it -- it doesn't cause an increased type 2 error rate. I would need to really see it done to be able to see that.
Q. Have you ever used the Holm Bonferroni in any of your research?
A. I have not.
Q. Do you have any other experiences with the Holm Bonferroni correction?
A. I do not.

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Q. I'd like to introduce what's been marked as Exhibit MK11.
(Marked Exhibit MK11.)
BY MR. WONE:
Q. Do you see that, Dr. Kurzer?
A. I do.
Q. Do you recognize the document in Exhibit MK11, Doctor?
A. No, I don't.
Q. For the Madison Memory Study, have you ever seen data for any of the AD8 groups listed in Exhibit MK11?
MS. METZINGER: Objection to form.
THE WITNESS: The manuscript shows the 0-1 and the 0-2. And then I think we also saw the 3-5. I don't recall seeing the other data.
BY MR. WONE:
Q. How about outside of the manuscript? Have you seen any of the other AD8 groups besides the ones you just mentioned?
A. I don't recall. I don't recall seeing them.
Q. [redacted]

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[redacted]
MS. METZINGER: Objection to form.
THE WITNESS: [redacted]
BY MR. WONE:
Q. [redacted]
MS. METZINGER: Objection to form.
THE WITNESS: [redacted]
BY MR. WONE:
Q. [redacted]
MS. METZINGER: Objection to form.
THE WITNESS: [redacted]
BY MR. WONE:
Q. Yes.
MS. METZINGER: What was the

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question, Mr. Wone?
(Reporter read back requested material.)
MS. METZINGER: Objection to form.
THE WITNESS: [redacted]
BY MR. WONE:
Q. [redacted]
A. [redacted]
Q. [redacted]
A.
Q.
A.
Q. [redacted]
MS. METZINGER: Objection to form.

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THE WITNESS: [redacted]
BY MR. WONE:
Q. Do you know why the Madison Memory Study investigators would conduct all of the analyses in Exhibit MK11?
MS. METZINGER: Objection to form. Mischaracterizes the document.
THE WITNESS: So are you telling me that they did do all of these analyses? Is that what you're saying?
BY MR. WONE:
Q. Let's assume that they did. Do you know why the investigators for the Madison Memory Study would --
MS. METZINGER: I'm going to --
MR. WONE: -- analyses?
MS. METZINGER: I'm going to object to that question, Mr. Wone. If you want to make that representation to her, fine. But I would object to that question both as to form and on the grounds that it's misleading.

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BY MR. WONE:
Q. I'm asking you to make the assumption that they -- that the Madison Memory Study researchers did.
MS. METZINGER: And at what point in time?
MR. WONE: I'm sorry?
MS. METZINGER: At what point in time is Dr. Kurzer to assume that these analyses were conducted?
MR. WONE: Assume that they were conducted after the Madison Memory Study had been completed.
MS. METZINGER: Okay. And -- and how about in comparison with other analyses that may have been run and before or after the data was looked at?
MR. WONE: I'm not asking -- I'm not asking about other analyses. I'm asking about the ones in Exhibit MK11.
MS. METZINGER: And if you can -- if you're asking her a hypothetical, I would appreciate you completing that hypothetical so that Dr. Kurzer is aware of exactly the

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hypothetical that you're posing to her.
MR. WONE: I'm asking Dr. Kurzer assuming that the Madison Memory Study investigators completed the analyses displayed in Exhibit MK11 after the study was completed, do you know why they would do that.
MS. METZINGER: Are you saying after the study was completed but before any analyses were conducted?
MR. WONE: At any point after the study was completed.
MS. METZINGER: Okay. Well, I think those are two different scenarios.
MR. WONE: That's the scenario I'm asking.
BY MR. WONE:
Q. Dr. Kurzer?
MS. METZINGER: Well, I don't understand -- I don't understand the scenario you're asking. That's what I'm saying.
MR. WONE: I'm asking if any -- I'm asking -- saying assume that

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base -- the analyses in Exhibit 11 in MK11 were completed -- were conducted after the study was completed, does Dr. Kurzer know why these subgroup analyses would be done.
MS. METZINGER: Well, I'm going to continue to object on the fact that that's an incomplete hypothetical.
But, Dr. Kurzer, if you understand the question and you have an opinion on that, you can go ahead and answer.
THE WITNESS: Yes, I'll answer that.
I think that, Mr. Wone, if you really want the answer to that, you need to ask the people who did the study why they did those analyses. It does make a difference whether it was -- whether they were done in the original -- with the original data set or whether they were done after publication of the -- of the papers. That all would make a difference.
But, again, as a hypothetical,

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I'll respond to you with a hypothetical. I don't know why they did all of those analyses. I think that it's reasonable. They were very clear in the manuscripts and in the protocol that healthy people were their primary -- were their primary targeted population.
It's possible that they -- because they had people with more -- with higher cognitive dysfunction that they did some exploratory analyses for the purposes of seeing if it would be interesting to further study apoaequorin in people who have neurological dysfunction. That's a reasonable thing to do. They didn't publi- -- I'm not aware that they published these data, in which case they would have had to say -- should have said this is -- was this was a post hoc analysis which was not part of our original hypothesis.
But -- but it's very, very common to use a data set in order to

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generate other hypotheses to get a feeling for what else you might want to study. You have all this data. Why not look at it and see what's going on. Maybe you'll get a clue. And that could help put you in a new direction.
So I think that there are reasonable, acceptable reasons why they would have done those other analyses.
BY MR. WONE:
Q. Go back to your expert report, Exhibit MK1.
A. Okay.
Q. And go to page -- page 14, please.
A. Okay.
Q. In your report, you reached conclusions relating to vitamin D in cognitive function, correct?
A. Yes.
Q. Do you know when -- sorry. Does Prevagen contain vitamin D?
A. Yes, it does, I believe.
Q. And do you know when vitamin D first appeared in Prevagen?

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MS. METZINGER: Objection to form.
THE WITNESS: I don't recall when it was added.
BY MR. WONE:
Q. If you could look at paragraph 17 of your report, does that refresh your recollection as to when vitamin D was added to Prevagen?
A. Yes. 2016.
Q. Was vitamin D in the Prevagen that was used during the Madison Memory Study?
A. I don't believe so.
Q. If you could go back to the vitamin D section which was page 14.
A. Page 14.
Q. Yes.
A. 15.
Okay. I'm here.
Q. Did any of the studies cited in your report involving vitamin D use Prevagen?
A. No, they did not.
Q. Did any of the vitamin D studies used cited in your report include apoaequorin?
A. No, they did not.

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Q. If you could look at paragraph 61. It's on the bottom of page 15. Do you see that, Doctor?
A. I do.
Q. And does this paragraph list studies that you believe show beneficial associations between vitamin D and brain structure?
A. Yes.
Q. And what did you mean by "beneficial associations"?
A. What I meant was that vitamin D helps preserve healthy brain structure.
Q. What was the word you said after "helps"?
A. "Preserve" healthy brain structure.
Q. When you say "healthy, helps preserve," could you explain what you mean?
A. What I mean is that these studies showed that people with vitamin D deficiency had brain changes that reflect atrophy of the brain so that vitamin D deficiency is harmful to the brain. So in order to preserve brain structure, health -- a healthy brain

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structure, you would want to make sure not to be vitamin D deficient -- deficient.
Q. And is brain structure different from cognitive function?
A. Brain structure contributes to cognitive function so that brain atrophy would -- is certainly likely to have a negative affect on cognitive function.
Q. Can something preserve brain structure but not have any effect on cognitive function?
MS. METZINGER: Objection to form.
THE WITNESS: I couldn't answer that.
BY MR. WONE:
Q. How come?
A. I don't know the answer to that. Are there things that -- you know, are there specific examples of things that preserve brain -- are good for the brain or preserve brain structure but don't affect cognitive function? I'm not aware of examples of that. There may be some, but I'm not aware of them.
Q. Does having beneficial

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associations mean that vitamin D causes cognitive improvement in humans?
MS. METZINGER: Objection to form.
THE WITNESS: These studies alone do not prove that vitamin D improves cognitive function. These studies I listed here as part, again, of the totality of evidence showing that vitamin D has an effect on the brain because that's important to understand when you look at the other studies that I refer to later.
So I'm not suggesting that -- you know, all I'm suggesting is what I say, there's a beneficial association between vitamin D and brain structure. And so what we -- we know that vitamin D has an effect on the brain. There's no question about that. That's what I'm trying to get across here.
BY MR. WONE:
Q. And you mentioned vitamin D deficient. Is the effect the same in people who are not vitamin D deficient?

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MS. METZINGER: Objection to form.
THE WITNESS: That I don't know because these five studies that I cite all use vitamin D deficient people. So I can't reach a conclusion about that question.
BY MR. WONE:
Q. Okay. If you could go to paragraph 63.
A. Mm-hmm.
Q. It's on the next -- on page 16 of your expert report.
A. Yes.
Q. And then in this paragraph you discuss cross-sectional studies; is that right?
A. That's right.
Q. And what is a cross-sectional study?
A. A cross-sectional study is a study that looks at one time point and evaluates the relationship in this context, the relationship between vitamin D levels in the people and cognitive function at one time point.
Q. And when you used the phrase

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"beneficial associations" in paragraph 63, what did you mean?
A. What I meant is that vitamin D helps that -- in the case of the enhanced study, low levels of vitamin D were significantly associated with increased risk of cognitive impairment. So vitamin D is negatively associated with cognitive function. Excuse me. Wait a second. I said that wrong. With cognitive impairment. Vitamin D levels are positively associated with cognitive function so that low levels of vitamin D are associated with lower cognitive function or more cognitive impairments.
Q. Lower levels of vitamin D are associated with cognitive impairment?
A. Yes.
Q. Is that what you said?
A. Yes.
Q. Does that mean -- do these studies show -- do these studies in paragraph 63 show that increasing vitamin D improves cognitive function?
A. These are associate -- studies of association. So basically what they're saying is that there's an association between -- it's not

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causation, but there's an association between vitamin D levels and cognitive function particularly in the case of deficiency.
But in some of these studies, and I'd have to look at each study individually, the vitamin D levels may not -- may not have been deficiency. In other words, they may have done sort of a correlation where they look at the full spectrum of vitamin D levels and they see that the lower the vitamin D the poorer the cognition, and the higher the vitamin D the better the cognition.
Q. Do cross-sectional studies control for other factors that could influence the outcome?
MS. METZINGER: Objection to form.
THE WITNESS: In cross-sectional studies, most epidemiologists will control for as much as they can, so they will control for other factors that may affect cognitive function. For example, something like socioeconomic status would be something that might be controlled for in these studies. So they do control for

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factors that might confound the results.
BY MR. WONE:
Q. Would they control for factors that could affect someone's vitamin D levels like diet?
A. They should. They should. They should account for -- for things that affect vitamin D, other things that affect vitamin D levels, yes. But, again, I'd have to look at these studies. And I would -- I would suggest that it's very likely that the high quality papers did control for things or they would not have passed peer review and they would not have been published.
So, for example, in paragraph C on page 17, you can see that they adjusted for age, race, sex, body mass index, and education. So they adjusted for things that are well known to affect either cognitive function or vitamin D levels.
Q. And that study in paragraph C involved people who are vitamin -- involved vitamin D deficiency, correct?
A. Yes, they particular -- in

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particular, they focused on people who are vitamin D deficient.

Q. Do any of the studies cited in paragraph 63 show that vitamin D improves cognitive function?

MS. METZINGER: Objection to form.

THE WITNESS: No. As I said, this is an observational study which shows association. So lower vitamin D levels were associated with poorer cognitive function.

BY MR. WONE:

Q. Okay. If we could go to paragraph 64, please.

A. Okay.

Q. And in paragraph 64, you discuss studies that show beneficial associations between higher vitamin D intake and cognitive function, correct?

A. Yes, intake rather than levels.

Q. And what is the difference between intake and levels?

A. In a study in which they're looking at the relationship or the association

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between vitamin D levels and cognitive function, they're taking blood and measuring the amount of vitamin D in the blood. In the -- in the studies in paragraph 64, they're not measuring the vitamin D in the blood, they're measuring through questionnaires vitamin D intake. And they showed that a higher vitamin D intake was associated with better cognitive function.

Q. And is your -- when you said "beneficial associations" in paragraph 64, did you have a similar meaning as to when you said "beneficial associations" in your prior paragraphs in this section?

A. Yes. What I meant was that higher vitamin D intake is associated with better cognitive functioning. Lower vitamin D intake is associated with poorer cognitive function.

Q. And do any of the studies in paragraph 64 show that vitamin D -- increasing vitamin D improves cognitive function?

A. They show association, not causation.

Q. Do any of the studies cited in paragraph 64 show that vitamin D -- increases in vitamin D causes improvement in memory?

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A. I'd have to look at the studies again to be reminded of exactly which cognitive function tests that they did. In this -- for this review of the literature, I looked at many aspects of cognitive function, so it's very likely that memory was -- was part of what they were -- what they were evaluating.

Q. When I asked about cognitive function, you said that the studies in paragraph 64 did not show causation, they showed --

A. Right.

Q. -- association.

A. That's right. They don't show causation, the show association. That's correct.

Q. And so -- and so I -- my second question was, do any of the studies in paragraph 64 show causation in terms of improving memory or is it just association?

A. Again, my response would be that they don't show causation. I wouldn't say just association because I think association is important. I think that these studies are important as part of the totality of the data. Otherwise, they wouldn't be published if they were

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meaningless. So I think that the data are important and significant, but they do not show causation. I agree with you on that.

Q. All right. If we could go to paragraph 66. It's on page 21. Do you see that?

A. Yes, I do.

Q. And in this paragraph, in paragraph 66 of Exhibit MK1, you mention -- you used the phrase "prospective studies." Do you see that?

A. Yes.

Q. And what is a prospective study?

A. A prospective study is a study in which you do your measurements before people -- you do your measurements at the point when, as far as you know, everyone is healthy. And then you follow them over some period of time either by giving an intervention or by observing them to see if there are groups of people who may have had -- experienced cognitive decline, and then you look back and what their measurements were before they became -- before their cognitive function declined. And so these kinds of studies are considered much -- to provide much stronger data than the cross-sectional studies because it --

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they're not looking at one time point, they're looking at a change over a long period of time.

Q. And do you agree that the studies you cited in paragraph 66 relate to association not causation?

MS. METZINGER: Objection to form.

THE WITNESS: So this is -- this is a little bit more nuanced, the interpretation of these kinds of studies. They are observational. They are very, very strong observational studies. They are the best kind of epidemiological studies that can be done. And although they -- the data are not as strong as randomized clinical trials in certain ways, in other ways they're better because clinical trials have limitations. And I -- I know that the RCT is considered the gold standard, but there is a great disagreement about that.

There are epidemiologists who will tear clinical trials to shreds because of limitations in clinical

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trials. You have a smaller group. You might not be capturing people who respond to the drug. You're isolating this and it's not in a real-world situation.

So prospective studies like this are looking at enormous numbers of people in real-life situations, and that is a tremendous strength above that of a randomized clinical trial. So the dogma is that prospective study -- prospective epidemiological studies don't show causation and randomized clinical trials are necessary to show causation, but they both have strengths and they both have weaknesses.

And I would say that when you have ten or 15 prospective studies that all point to the same thing, that that is very, very strong data in the direction of causation, although technically the dogma would say you cannot say that that shows causation. To me, it's very strong data.

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BY MR. WONE:

Q. And the studies cited in paragraph 66 relate to vitamin D levels, not supplementation, correct?

A. That's correct, I don't believe any of them were supplemented. I don't believe any of them were supplemented.

Q. So during the course of the studies, none of the participants in the studies cited in paragraph 66 took vitamin D as part of the study?

A. Not as part of the study, but they may have been taking it on their own. That's -- that's very possible. And that's why it's a real-world situation.

Q. Okay. If we could go on to paragraph 67. It's on page 26.

A. Okay.

Q. And in this paragraph, you also discuss prospective studies, correct?

A. Yes.

Q. And you used the phrase "beneficial associations"?

A. Yes.

Q. And does that have -- does that

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phrase have the same meaning?

A. Yes. Higher vitamin D consumption was associated with better cognitive function. And in this case, there are some randomized clinical trials that are included in this because they are a type of prospective study in which you give a treatment to the person and then see what the impact of that treatment is rather than measuring their natural levels and following them over time.

Q. And is the study mentioned in paragraph 67B one of the RCT studies you mentioned?

A. Did you say B or D?

Q. B as in boy.

A. B as in boy.

Yes. So study -- the study in b, study b is a double-blind placebo-controlled RCT.

Q. Okay. I'd like to introduce what's been marked as Exhibit MK12.

(Marked Exhibit MK12.)

BY MR. WONE:

Q. Do you see that exhibit, Doctor?

A. I do. I'm going to open it

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right now.
Okay.
Q. And is the study in Exhibit MK12 the study you were referring to in paragraph 67B of your expert report?
A. Yes.
Q. And I'll refer to this as the Grung study, if that's okay.
A. As the what?
Q. As the Grung study?
A. The Grung study, yes. Yes.
Q. Did the Grung study look at vitamin D deficient adolescents?
A. I don't believe that they were deficient. I think they were Norwegian adolescents broken into two groups who either consumed vitamin D or not. This is a little bit small on my screen, so I'm trying to...
Q. There's a magnifying glass in your viewer you can use to increase it.
A. Okay. Here we go. Got it. Thank you. Thank you so much. That really helps.
So there were 50 adolescents who were assigned -- randomly assigned to either take vitamin D or placebo and -- so that they were not

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recruited to be vitamin D deficient. They went -- when they measured the -- the vitamin D, it turned out that the -- the average consumption was deficient, but it doesn't look to me that they intentionally recruited deficient participants.
Q. But the participants were deficient?
A. Yes.
Q. Vitamin D deficient?
A. Yes. And that reflects the population at large because in Scandinavia and in the United States, there is a huge problem with vitamin D deficiency. So it's not at all surprising that when they recruited these healthy kids, that many of them were deficient.
Q. Are adolescents the target audience for Prevagen?
A. No, they're not.
Q. And do adolescents typically experience age-related cognitive decline?
A. No, they don't.
Q. How about mild cognitive impairment?
A. No, they don't. Again, this paper was cited to give the view of the totality

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of the evidence showing that vitamin D seems to have an impact on cognitive function and brain function. I think that most of the papers that I have referred to were in the target population. There may be a few that were not. And I included them just because it's more evidence to show that vitamin D does have this effect. But most of the papers that I -- that I -- the vast majority of them are in the target population.
Q. And could there be cognitive function differences between adolescents and older adults with age-related cognitive decline?
MS. METZINGER: Objection to form.
THE WITNESS: Can you rephrase that, please?
BY MR. WONE:
Q. Are there differences in the cognitive function of adolescents versus older adults with age-related cognitive decline?
MS. METZINGER: Objection to form.
THE WITNESS: I would suspect so. I can't answer conclusively that question, but I would suspect that

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that's the case, that there are differences.
BY MR. WONE:
Q. And is the reason why you can't answer conclusively because cognitive function is not your expertise?
MS. METZINGER: Objection to form and argumentative.
THE WITNESS: The reason I can't answer is because I'm not familiar with this particular question, which is the difference in cognitive function between adolescents and adults with cognitive decline. There may be experts in cognitive function who aren't aware of that, and so it's -- it's -- I'm just not aware of that particular question that you asked.
BY MR. WONE:
Q. Okay. If you could go back to paragraph 67 of your expert report, please.
A. Yes.
Q. Are there any other RCT studies cited in paragraph 67 that would show that taking vitamin D improves cognitive function?

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A. Yes, I believe that there are.
Q. And which ones? If you could point me to the paragraph.
A. 67c, this was an RCT of over 18 weeks of 82 healthy adults who were supplemented with either 400 or 4,000 international units of vitamin D. They had two doses, which is an extremely sophisticated way to do a study if it's -- if -- if you have the resources to do a dose-response study. So they wanted to look at both of these two different doses. And they found that -- that there were improvements in cognitive function in the high-dose group. And the improvements were greater in people who had lower levels at baseline.
So there was improvement in the high-dose group as a whole, but the improvements were better in those with -- who started out with lower vitamin D. They did not see this effect on nonverbal memory in the low-dose group.
Q. And do you know the amount of vitamin D in the high-dose group in the study that you're referencing in paragraph C?
A. 4,000 international units.

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Q. And how much vitamin D is in Prevagen?
A. 2,000 international units.
Q. So the dose -- the high-dose used in that RCT in paragraph C was more than what is contained in Prevagen, correct?
A. Yes, that's correct.
Q. Was there a placebo group in the study that's -- that you're referring to in paragraph C?
A. There was not a placebo group. There were -- there were two test groups. And so the lower group took 400, the higher group took 4,000. So there was not a zero -- a zero group.
Q. Okay. Are there any other studies in paragraph 67 that you would say show that vitamin D improves cognitive function?
A. So in 67D, this is an RCT of 181 participants who have mild cognitive impairment, and they were randomized to receive either 400 IUs or placebo for 12 months and they -- these -- those researchers saw a significant improvement in cognitive function in the vitamin D supplemented group. And you'll note that this was published in one of the best neurology journals that exists.

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Q. And the participants in the study that you're referring to in paragraph D, they had mild cognitive impairment, correct?
A. Yes, they did. Yes, they did.
Q. And do you know what cognitive function measure was used in that study?
A. I'd have to look at the study. I don't recall right now.
Q. I'm marking what's introduced as Exhibit MK13.
(Marked Exhibit MK13.)
BY MR. WONE:
Q. Do you see that, Doctor?
A. Yes.
Q. And is this the study that you were referring to in paragraph 67D?
A. Yes, it is.
Q. And what cognitive function measure was used in Exhibit MK13?
MS. METZINGER: Mr. Wone, your voice dropped a bit during that question. Can you repeat it, please?
MR. WONE: Sure.
BY MR. WONE:
Q. What cognitive function or --

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I'll start again.
How was cognitive function measured in the study in MK13?
A. It was -- the main outcome was evaluated using the Chinese version of the Wechsler Adult Intelligence Scale-Revised. And so they had 11 tests that evaluated -- hang on a second. Yeah, cognitive domains were evaluated using 11 different tests involving vocabulary, comprehension, arithmetic, digit span, et cetera.
Q. And do you know whether the Wechsler Adult Intelligence Scale-Revised tests memory?
A. I don't know. I don't know the answer to that. They also used the Mini-Mental State Examination, which is very, very frequently used as a measure of general cognitive function. Again, offhand, I don't recall if memory is a focus of that.
But there's no question that memory and cognitive function are very, very intertwined. You know, memory is a part of cognitive function. Memory affects cognitive function. I'm not sure that you can actually separate them very well.

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Q. Did the study in Exhibit MK13 mention any results for the -- that second measure you mentioned, the Mini-Mental State Examination?

A. Hang on a sec.

I don't see it referred to.

Hang on a second. I don't see them referred to those results.

Q. Going back to paragraph 67 of your expert report, are there any other studies that you would say show that vitamin D intake improves cognitive function?

A. Yes, there's one more. I do want to -- if I -- if I might make a comment on the previous study.

Q. Sure.

A. As I -- as I said a few minutes ago, that study was published in a very, very high-quality clinical neurology psychiatry journal. And assuming that the peer review is excellent, which I think is a reasonable assumption with a journal of that quality, then I would assume that the methodologies that were used were very likely to be appropriate for that population. So I just wanted to point that out.

Q. Okay.

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A. The next one is E?

Q. Yes.

A. An RKTC performed in 55 overweight or obese women, 58 years, with low vitamin D levels. They took either 600, 2000, or 4,000 IUs for one year and cognitive testing was done at the end of the year.

Q. So this study involved overweight or obese women, correct?

A. That's correct. That's correct.

Q. And the -- and the women were -- had vitamin D deficiencies?

A. You know, there's some argument as to where 30 is a cut- -- is actually -- would fall within the vitamin D deficient. It's certainly on the low side. But some clinicians would consider that deficient and some clinicians would not.

And the other thing that I want to point out about this trial and the other trial that did not have a placebo, it's possible that the researchers -- and I've been involved in studies for which this was the case, or at least I've been involved in discussions of studies where this was the case. The researchers may have felt

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that it was unethical not to give everyone vitamin D because it's such an important nutrient. So many people are -- are deficient and it's such an important nutrient for older women because of its importance in bone health, particularly. So they may have felt that they really needed to give -- that it was not ethical to have a zero group because they would have had to tell woman who were already taking vitamin D to stop taking it, and that would probably be viewed as unethical and it wouldn't get past the -- the Institutional Review Board.

Q. Okay. If we could turn to paragraph 68.

A. Yes.

Q. You mentioned a case control study --

A. That's right.

Q. -- that show beneficial associations between higher vitamin D levels and cognitive function. Do you see that?

A. That -- that's right, yes.

Q. And does the case control study cited in paragraph 68 show that vitamin -- taking vitamin D causes improvement in cognitive

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function?

A. Again, this is a study that shows association, so it is -- this -- and these kinds of studies have fallen out of favor a little bit because there are too many confounders with these retrospective case control studies. And so I threw this study in here just to add to the data, but I would say that this is not one of the stronger studies that -- that we've -- we're discussing today. But they did show that using -- they used electronic medical records and they showed that -- that people with dementia tended to have lower levels of vitamin D.

Q. Okay. And in paragraph 69, you state that meta-analyses that show beneficial association between higher vitamin D levels and cognitive function. Do you --

A. Mm-hmm.

Q. -- see that?

A. Yes.

Q. And do any of the meta-analyses cited in paragraph 69 show that taking vitamin D causes improvement in memory?

A. No. Let's see. A is cross-sectional associations, B is cross-sectional

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and longitudinal. Then there's a systematic review. Observational with three interventional studies. So the interventional studies are the ones that are generally considered to show causation. The observationals are generally considered to show -- to show -- to show association. And so the -- the -- whether the meta-analyses can show or prove, as you say, causation versus association depends on what kinds of studies were included in the metanalysis. And it looks as the -- as though most of these were -- were observational studies, and so they have all of the strengths and limitations of other observational studies, only increased power to see a different -- to see a change or an effect.

MR. WONE: Can we go off the record for a moment?

THE VIDEOGRAPHER: We are going off the record at 4:09 P.M.

(Off the record from 4:09 until 4:10.)

THE VIDEOGRAPHER: We are going back on the record at 4:10 P.M.

BY MR. WONE:

Q. If you could turn to

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paragraph 78 of your report, Doctor, please.

A. Yes, I'm there.

Q. And in your -- in the first sentence, you state that it's your expert opinion that a supplement containing 500 to a thousand IUs per day would be sufficient to achieve cognitive benefits. Do you see that?

A. Yes, I do.

Q. And what cognitive benefits were you referring to?

A. I'm referring to in this case numerous cognitive benefits, including memory.

Q. Does any of the evidence in Section 10 of your report show that vitamin D causes improvement in any aspect of cognitive function?

A. Can you say -- re- -- can you rephrase that question, please?

Q. Does any of the evidence that you cited in Section 10 of your report show that vitamin D causes improvement in any aspect of cognitive function?

MS. METZINGER: Objection to form.

THE WITNESS: Yes, I believe

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that it does. There are some randomized clinical trials that show improvement. And then there is an enormous amount of epidemiological data showing very strong associations, and that data should not be ignored. And so I consider that data. And I know that -- that, you know, there -- there may be others who don't.

But I think that when you have an enormous amount of epidemiological data, it really points in the direction, especially when it's -- when they're very well-done prospective studies, they certainly point in the direction of causation. They don't prove it, but they provide very, very strong evidence.

And so I do believe that the data that I have summarized shows that vitamin D supplementation will help with cognitive benefits, including memory.

BY MR. WONE:

Q. And when you say "will help with

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cognitive benefits," do you mean that it causes improvement in memory?

A. Yes. Yes. And -- and, again, you know, as we -- as I said before, I -- I -- I hope it's okay that I'm kind of repeating myself. I think that this threshold of evidence is intended to be different by regulators for dietary supplements than for drugs. And if this were a drug that was being evaluated, particularly a drug that had potential very harmful side effects where you have to be really careful with it, then the -- my threshold for evidence might be higher. For a dietary supplement which has no adverse events which is very likely to cause improvements for people, in my opinion this evidence meets that threshold.

Q. And what is the basis for your belief that the standard for dietary supplements is different?

A. Because in -- in the early 1990s, the Dietary Supplement Act was created in order for dietary supplements to be regulated differently than drugs and foods, and particularly differently than drugs. And so -- and in the guidance, as I said before, there are parts of the

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guidance that you can pull out that very clearly intend there to be flexibility in interpreting data, flexibility in applying data that they are -- if they wanted these trials of dietary supplements to be held to the same standards as drugs, they would not have created separate regulation for supplements.

Q. Can a dietary supplement have a harmful effect?

MS. METZINGER: Objection to form.

MR. de LEEUW: Do you mean -- I'm going to object as well. I mean, maybe you want to put a little meat on that question.

BY MR. WONE:

Q. Do you understand my question, Doctor?

A. Yes. You asked if it's possible that there could be dietary supplements that have harmful effects. Yes, it is possible. And even -- even with, as I said, the green tea trial, the green tea catechin supplements are known to have potentially harmful effects on the liver. But in our study that we did, our clinical trial,

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we looked at that, and it was determined, and the data and safety monitoring board agreed with it, that the level of adverse events was so low that it was nothing to be concerned about.

So in general, I think we think of dietary supplements as supplements that are very safe.

Q. Would you go to paragraph 84 of your report, Exhibit MK1, please.

A. Yes.

Q. In the second to last sentence, you used the phrase "reasonable degree of scientific certainty." What did you mean by that?

A. Which -- which -- are we in 80? In paragraph 80?

Q. I'm sorry. Paragraph 84.

A. Oh, I'm sorry. Paragraph 84.

Q. Sorry, Doctor.

A. Okay. On page 35 -- or 37. 35.

Q. You used the phrase "reasonable degree of scientific certainty" --

A. Yes.

Q. -- on the second to last line.

A. Yes.

Q. What did you mean by that?

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A. What I mean by that is that I don't think that we can ever be 100 percent certain of anything in life, including science. And so I am being honest here in saying that I am not a hundred percent certain, but I think that I have a reasonable degree of scientific certainty, meaning I believe that there's enough evidence that the statements are supported by competent and reliable scientific evidence.

Q. And when you say "statement," you're referring to -- are you referring to the challenge claims?

A. Yes.

Q. Could you quantify what you mean by what is a reasonable degree of evidence?

A. I --

MS. METZINGER: Objection --

THE WITNESS: -- can't quant- --

MS. METZINGER: -- to form.

THE WITNESS: Go ahead.

MS. METZINGER: Objection. Objection to the form.

Go ahead, Dr. Kurzer.

THE WITNESS: I can't -- I can't quantify that. You know, this is

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basically saying that it's my judgment as a scientist, as, you know, a leader in my field, it is my judgment that the evidence is supported, that the evidence supports the claims. That's what I'm saying. I can't quantify it. I can just say that I with my judgment and my background, my knowledge, my experience, I can say that I believe these statements to be valid.

MR. WONE: Okay. Could we go off the record?

THE VIDEOGRAPHER: We are going off the record at 4:18 P.M.

(Off the record from 4:18 until 4:40.)

THE VIDEOGRAPHER: We are going back on the record at 4:40 P.M.

MR. WONE: Thank you for your time this afternoon, Dr. Kurzer. We don't have any further questions.

And I will turn it over to co-counsel, Kate Matuschak.

THE WITNESS: Thank you, Mr. Wone.

EXAMINATION
BY MS. MATUSCHAK:
Q. Good afternoon, Dr. Kurzer.
A. Good afternoon, Ms. Matuschak.
Q. So as you know, my name is Kate Matuschak, and I am co-plaintiff with the Federal Trade Commission on behalf of the New York State Attorney General's Office, and I just wanted to ask you a few questions.
Could you please turn to paragraph 56 of your report, which is Exhibit 1. It's -- it's on numbered page 13, which is --
A. Yes, I see.
Q. Great.
A. Mm-hmm.
Q. And in the first line of paragraph 56, you say "I believe that it is unlikely that intact AQ is absorbed and enters the brain."
Is "AQ" apoaequorin in this context?
A. Yes, it is.
Q. Okay. And why do you believe that it is unlikely that intact apoaequorin is absorbed and enters the brain?

A. Generally large molecules like apoaequorin are not -- do not pass the blood brain barrier. I've subsequently learned that there are mechanisms through which apoaequorin can combine with cholesterol and that there are examples of other large molecules that are able to get past the blood brain barrier this way, making them more lipophilic. So I might modify that and say that -- I mean, I still believe it's unlikely, but I think it's more plausible than I -- than I thought when I wrote the report.
Q. Okay. But you did not offer the opinion that you believe the mechanism by which apoaequorin active -- by entering the brain, correct?
A. That's correct.
Q. And are you aware of the theory that apoaequorin can exert effects on the brain because of its calcium binding properties?
A. Yes. I understand that those were the original -- I think that those were the original hypothesis about how apoaequorin might exert its effects.
Q. And whose hypotheses were those?
A. I believe that they were the

hypotheses of Moran and the authors of the earlier papers on apoaequorin in -- in vitro and in vivo.
Q. Do you recall the authors of any of those earlier papers?
A. Right now, I don't.
Q. Okay.
A. I think -- you know, Moran I know for sure is one. And the others I don't recall right offhand. I'd have to look at my reference list.
Q. So for apoaequorin to have this calcium binding effect, it would need to be in the brain intact. Would you agree with that?
MS. METZINGER: Objection to form.
THE WITNESS: I would say that that's -- it's possible that that's true. It's also possible it's not true because if there are segments of apoaequorin that are released in di- -- during digestion, they might -- the segments might be able to enter the brain and exert this effect. So there are other plausible mechanisms besides that the whole molecule of apoaequorin

enters the brain.
BY MS. MATUSCHAK:
Q. Right.
But the question is just about the calcium binding. So my question is, would intact -- the full protein intact need to be present to have a calcium binding effect?
A. And what I'm saying is I don't know.
MS. METZINGER: Objection to form.
Go ahead.
THE WITNESS: Hmm?
MS. METZINGER: I just objected to the form. But you can go ahead, Dr. Kurzer.
THE WITNESS: I'm sorry.
MS. METZINGER: That's all right.
THE WITNESS: I'm falling into thinking this is just a conversation between friends.
What I'm trying to say is that it's possible that there are segments of apoaequorin that are released during

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digestion that have calcium binding properties and that perhaps they could move into the brain and exert a calcium binding effect.
BY MS. MATUSCHAK:
Q. What --
A. And I -- I -- I don't -- I'm just -- I'm just hypothesizing something that could be plausible.
Q. And what's the basis for your belief that that is plausible?
A. The basis of my belief is basic understanding of digestion and physiology of many substances and the fact that we know that there are metabolites of other substances that do go into the brain even though the whole substance cannot. And so it's not based on evidence. It's not based on studies that have been done. It's just a possibility.
Q. Okay. So just to be clear, you're not referring to any evidence that there is some --
A. That's --
Q. -- derivative --
A. -- right.

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Q. -- of apoaequorin that has a calcium binding effect?
A. That's right. That's right.
MS. METZINGER: Objection to the form.
BY MS. MATUSCHAK:
Q. And later on in this paragraph 56 in your report, you discuss gut-brain axis theory, correct?
A. Yes, I do.
Q. And if you could just turn to page 14 where the paragraph spills over. In the third --
A. Yes.
Q. -- line -- in the third line down, you refer to peripheral intestinal substances. What do you mean by that phrase?
A. What I mean is by -- that there are dozens and dozens and dozens of substances that are synthesized in the gastrointestinal tract, in the stomach and largely in the small intestine, so some degree in the large intestine, that exert an effect on the brain.
In fact, the gastrointestinal tract is considered by some people to be the

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largest endocrine organ system in the body. And this is fairly new knowledge. It's just the last few decades that we've understood this, that -- that we have -- that there is a very clear pathway - and there's no debate about this in the nutritional science world in which I reside, there's no controversy about this - substances, hormones are secreted in the -- In the gastrointestinal tract?
The best understood relate to how we control food intake. How is food intake controlled. How is it that we stop eating when we've had -- we've eaten enough food. Well, one thing is the stomach gets full and we feel a little bit fuller. That's part of it. But in addition, there are hormones that are secreted by the -- by the cells of the stomach and the cells lining the small intestine that -- that attach to chemoreceptors on the vagus nerve which travels from the intestine to the brain, and they actually exert effects on the center in the brain which is responsible for appetite.
So we -- we very quickly have a regulatory system that tells us when we're -- when we should be hungry because there hasn't been any

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food in a while or when we should be -- when we should stop eating because we've eaten recently. And it's these -- these chemical secreted in the gastrointestinal tract that -- that signal the -- the nervous system through the vagus nerve which then signals the -- the hypothalamus, the cells in the appetite center. So this is well known. We've known this a few decades.
But there are other substances as well. Serotonin is secreted in the gastrointestinal tract, and we know that serotonin is a brain bioactive. And there are many, many other examples of -- of neurotransmitters and hormones that we know are active in the brain that are actually secreted in the gastrointestinal tract. So this is something that's very, very well known, and I would say that we're getting more and more and more and more data on this all the time.
And the most recent --
Q. Thank you. Thank you, Dr. Kurzer.
A. Okay.
Q. I'm sorry. I just -- we're running short on time, so I --

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A. Sorry.
Q. -- just want to make sure I cover the -- the topics --
A. Okay.
Q. -- I want to cover.
A. I'm sorry.
Q. So I'm sorry to cut you off. I just would just ask if you could just answer the question. And -- and, you know, if your attorneys want to ask you questions if you want to add anything at the end, they can do that.
A. Okay.
MR. de LEEUW: I object to that characterization. She was actually answering your question.
MS. METZINGER: I agree with that and second that, Mr. de Leeuw. Thank you.
BY MS. MATUSCHAK:
Q. So I would like you to look at paragraph 57 on this page 14 of your report.
A. Yes.
Q. And I just want to clarify. The references cited in this paragraph, number of them address apoaequorin specifically, correct?

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A. Right, yes.
Q. And none of them address products of apoaequorin specifically --
A. That's correct.
Q. -- correct?
A. That's correct.
Q. No -- so no peptides derived from apoaequorin are addressed in these references?
A. That's correct.
Q. And so none of them demonstrate any bioactive peptides resulting from apoaequorin, correct?
A. That's correct.
MS. METZINGER: Objection. Objection to form.
BY MS. MATUSCHAK:
Q. I'd like you to turn now to paragraph 82 of your report. And that's page -- it's numbered page 35, which I believe is page 37 of this exhibit.
A. Is this the bibliography?
Q. Oh, I'm sorry. We may not be on the page.
MR. de LEEUW: What's the

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paragraph number? What's the paragraph number?
MS. MATUSCHAK: Paragraph 82.
THE WITNESS: I have it.
MR. de LEEUW: Paragraph 82. It's on -- okay.
THE WITNESS: I have that.
MS. MATUSCHAK: Okay. Great.
BY MS. MATUSCHAK:
Q. So in the fourth line of this paragraph, you say "substances in the GI tract can signal the brain through the vagal nerve and/or gut microbiota." And this is the theory you were just describing in your last answer, correct?
A. Yes.
Q. I'm sorry, not in your last answer but in your discussion of paragraph 56, the gut-brain axis, correct?
A. Yes.
Q. So are there -- does this mean there are two parts to your gut-brain axis theory, one involving vagal nerve and the other involving gut microbiota?
MS. METZINGER: Objection to form.

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THE WITNESS: This is exactly where I was going when I was talking a little bit too much a few minutes ago.
BY MS. MATUSCHAK:
Q. Okay.
A. The more recent understanding of the gut-brain axis is that the microbiota are extremely active that the -- that there are -- that there are compounds synthesized by the bacteria in the gut, including serotonin and a number of hormones are synthesized by the bacteria. So the bacteria are -- they secrete and synthesize very, very bioactive compounds. And this is very, very new, exciting work that's being funded at enormous levels at the -- by the federal government because we now know that the microbiome really has a huge impact on health.
Q. And you haven't cited any evidence that apoaequorin can have an effect via the gut-brain axis theory, correct?
A. That's correct.
MS. METZINGER: Objection to form.
THE WITNESS: I haven't. And my understanding of the guidance is that a

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mechanism is not required. And that's why, despite the fact, that I haven't identified a mechanism for sure for apoaequorin because there are plausible mechanisms. My interpretation of the FTC guidance is that the -- the -- this is acceptable evidence, the fact that there are plausible mechanisms.

BY MS. MATUSCHAK:

Q. So in -- back to paragraph 82, in the fifth line down, you say "products of AQ," apoaequorin, "digestion in the stomach and intestine could be absorbed and exert effects on the brain." This is your bioactive peptide theory, correct?

A. Yes.

Q. But you don't -- as -- as I think we've established, you don't -- you haven't cited any evidence that apoaequorin actually produces bioactive peptide, correct?

A. That's correct.

MS. METZINGER: Objection to the form.

BY MS. MATUSCHAK:

Q. Okay. I'd like to go back now

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to paragraph 56 of your report. So paragraph 56 where you discuss the gut-brain axis theory, you cite a biochemistry textbook, correct?

A. Yes, I do.

Q. And you believe that this is a good reference to rely upon in general?

A. In general, it's a -- it's a good reference. It is an old reference and probably outdated. And I know that I made a mistake with that reference. And I think the reason is because -- I actually wrote three or four different reports that got merged into one report, and I had to redo all of the references in order to create one report. And it is very possible that there was some kind of a mistake made with the reference because of that. So I apologize for that error.

Q. No need to apologize. I just want to make sure I understand, you know, the -- the basis for -- what you're citing as the basis for the gut-brain axis theory.

A. There are lots I could provide, if you were interested, lots of other references. So, really, I chose -- you know, in -- in many of the points that I'm making, there are multiple

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references that could be cited. And in this case, I certainly could provide other -- additional references.

Q. But here you cite just the biochemistry book, correct?

A. That's correct. But it's a mistake. As I said, I think some references got mixed up and that -- that is not the correct reference for that comment.

Q. But you would agree that this reference doesn't support the statements in this paragraph?

A. Yes.

MS. METZINGER: Objection to form.

BY MS. MATUSCHAK:

Q. And were you familiar with Dr. Berg, Dr. Jeremy Berg, before your work on this case?

A. No.

Q. And in paragraph 57, I believe you also cite Dr. Berg's book, and I'll just point you to it. It's in the fifth line of that paragraph.

A. Same problem. This -- this

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reference got put in there and it shouldn't have been. And I think it was the work -- it took me many, many hours to redo all of the references when the reports got merged, and so the wrong reference was put here. So that reference that's cited does not support that sentence. But as I said, I could provide other references that would. And, frankly, that 20 -- that 20-year-old textbook is probably outdated, so I -- it would also be interesting to look at a more current version of it to see if they include these statements.

Q. You don't cite any evidence of amino acid small peptides containing, say, four or more amino acid units that are -- that can be absorbed in the small intestine, correct?

MS. METZINGER: Objection to the form.

THE WITNESS: I -- I may not have a citation here, but there certainly are some that I know of and that I could easily provide references for. For example, lunasin is a peptide found in soy protein, which is 43 amino acids. And there have been studies done because it's been shown to

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exert anticancer properties, so there's a lot of interest in it. There have been studies done where people have been given lunasin and it's measured in the blood. That shows --

BY MS. MATUSCHAK:

Q. But you don't --

A. -- it's absorbed.

Q. But you don't refer to that in your report, correct?

A. I don't. I don't, no.

Q. Did you review the -- the report of Dr. Jeremy Berg that was submitted in this matter?

A. I did.

Q. Did you consider offering a rebuttal opinion to that report?

MS. METZINGER: Objection. I'm going to instruct the witness not to answer that question on the grounds of attorney-client privilege and work product.

BY MS. MATUSCHAK:

Q. Are you going to follow that instruction?

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A. I am.

Q. Would you consider yourself to be a biochemist?

A. I am a nutritional scientist, and biochemistry is a fundamental -- a fundamental -- it's a foundational discipline for nutritional science. Nutritional science is basically a combination of biochemistry and physiology as it applies to nutrition and to nutrients. How are they absorbed, how are they digested, what happens to them after, what about metabolism, these are things that I'm an expert in.

And I have, as a nutritional scientist, I think a much broader understanding of nutrition and what happens to things that we consume than many biochemists who have -- tend to have very, very narrow approach, very narrow understanding of their particular field of expertise.

So I am not trained in biochemistry at the Ph.D. level. I do not have a Ph.D. in biochemistry. I have taken many biochemistry classes. I have taught biochemistry classes. And I certainly consider myself to be an

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expert in nutritional biochemistry.

Q. And, yes, I appreciate that background, and I heard a lot of it earlier on today when we were talking about your background in general.

The question is simply would you consider yourself to be a biochemist.

MS. METZINGER: Objection. Asked and answered.

THE WITNESS: As I said, I consider myself to be a nutritional scientist. I have an expertise in nutritional biochemistry, yes. I know more nutritional biochemistry than most biochemists do.

BY MS. MATUSCHAK:

Q. Other than reviewing literature, do you have any experience studying the mechanics of protein digestion?

MS. METZINGER: Objection to form.

THE WITNESS: Can you explain what you mean by "experience"?

BY MS. MATUSCHAK:

Q. Any -- any type of study of --

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of the mechanics of protein digestion.

A. I have not done studies on protein digestion. I have done studies on -- in fact, I was involved in studies that were done at UC Berkeley on the protein requirements of women. And, in fact, they're cited in the international guidelines for protein requirements. And so I've been involved in studies that looked at whole body protein utilization. I have not done studies on protein digestion per se myself.

Q. And other than reviewing literature, do you have any experience studying the mechanics of protein metabolism?

MS. METZINGER: Objection to form.

THE WITNESS: I have not performed research on protein metabolism, but I have taught it to graduate students at the University of Minnesota. So I have enough of an understanding of the literature and the most current information that I can -- that I can teach classes on that involve protein digestion and protein utilization. I have not done research

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on that myself.
BY MS. MATUSCHAK:
Q. Can you tell me the general subject matter of the classes that you taught that involve protein metabolism or protein digestion?
A. I teach an introductory nutrition class which is an overview of all nutrition, and we go through every nutrient category in great detail. Two weeks ago I gave a lecture to University of Minnesota students, to 150 students, on digestion and absorption. And then as we talk about each category of macronutrients when we -- when we talk about protein, which we'll be doing I think next week, then there will be lectures on pro- -- more deeper, a deeper look at protein digestion, absorption, metabolism.
Q. Anything other than the lec- -- the intro -- introductory nutrition class and --
A. I --
Q. -- the lecture --
A. Yeah, I've -- I've --
Q. Sorry. Go ahead.
A. I just didn't want to jump in too quickly.

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I have taught a class a number of times on protein and energy utilization where I focus on the relationship between protein needs and energy needs in humans, and so that's another class that I've taught. And I've taught a class on nutrition and endocrinology where I focus on -- and this is a high level class, this is for doctoral students, focusing on the hormones that influence nutrition and how nutrition influences hormones. So I do consider myself an expert in that subject.
Q. Have you ever conducted a study to determine whether a compound has entered the bloodstream?
MS. METZINGER: Objection to form.
THE WITNESS: Yes, I have. In the -- in the soy studies that I've done with soy protein, we have been very interested in bioactive compounds in soy protein called isoflavones. And I have done numerous studies in which we have given -- we have given people known amounts of isoflavones and then measured them in the blood and in the

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urine to evaluate the, you know, digestion and absorption.
BY MS. MATUSCHAK:
Q. And what was your role in that study?
A. Principal investigator.
Q. And do you have any other studies that -- in which you have studied whether a compound has entered the bloodstream?
A. In the green tea trial that I did which I also was a principal investigator of, we -- those are both -- these are all NIH-funded trials. We gave a capsule with a -- an extract of green tea that contains catechins, which are the bioactive compounds -- thought to be the bioactive compounds in green tea, and we measured -- we -- we gave people a known amount of catechins, and we measured them in the blood and in the urine. So we know that they were absorbed and we know how much they were excreted.
Q. Have you ever conducted a study involving a supplement that contains a protein?
A. I've done lots of studies with soy protein. So that is a protein. And in that case, it is a protein that contains bioactive

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substances in it that are released when it's consumed and when it's digested. The bioactive substances are released.
Q. Yes. But that is not a dietary supplement containing a protein, is it?
A. I don't know. I think you should give me an example of a dietary supplement containing a protein. Do you mean -- are you speaking about apoaequorin in particular that -- a dietary supplement that is a protein? Is that what you mean?
Q. Right, right. Well, I mean, I think you were speaking with Mr. Wone earlier about the difference between, you know, dietary supplements, studies involving dietary supplements in which you could have, you know, some people getting the placebo and other people getting the active ingredient versus studies involving food product where people know what they're getting. And so I'm trying to draw a distinction between those two in asking whether you've done any studies in which the active ingredient in a dietary supplement is a protein.
MS. METZINGER: Objection to form.

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THE WITNESS: No. Given the way that you're phrasing this question, my answer would be no. I have not -- you know, I've given -- I've done studies with supplements that were given as pills. They were not proteins.

BY MS. MATUSCHAK:

Q. Do you know how one might go about testing apoaequorin to determine what products result from digestion?

MR. de LEEUW: Object to form.

THE WITNESS: I think the best way to do that would be to do a human study in which you -- you -- you provide apoaequorin to people and then you -- you remove fluid from the stomach, from the small intestine, et cetera, to see what is released.

There are other ways to do this. You could use a radiolabeled apoaequorin where you have a -- you know, it's called a -- you know, not -- not radioactive but a heavy -- an isotope so that when apoaequorin is consumed, if it is absorbed, digested

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and parts of it are absorbed, you can measure this isotope in the blood and you can follow it to see where it goes.

So there are ways to do it. They're difficult studies, but it's possible to do those.

BY MS. MATUSCHAK:

Q. Are you aware of such studies being conducted by anyone?

A. I am not aware that such studies have been conducted. I'm also not aware that the FTC guidance requires those kinds of studies. So, you know, you're right, I don't think they've been conducted. But despite that, I still stand behind my conclusions.

Q. Just to be clear, you're not aware of any studies such as the ones you just described being conducted with respect to apoaequorin, right?

MR. de LEEUW: Objection.

THE WITNESS: Yes.

MR. de LEEUW: Object to --

MS. METZINGER: Objection.

MR. de LEEUW: -- the form of the question.

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MS. METZINGER: Asked and answered and to the form.

BY MS. MATUSCHAK:

Q. Have -- are you familiar with something called a PeptideCutter?

A. A PeptideCutter? I'm not familiar with that term. Yeah, I'm not familiar with that term.

Q. Okay. Are you familiar with an Expasy tool? It's spelled E-X-P-A-S-Y.

A. No, I'm not familiar with that.

Q. Are you familiar with high performance liquid chromatography or HPLC analysis?

A. Yes, I've used HPLC analysis and I've used -- that's liquid chromatography. I've also used GCMS, which is gas chromatography–mass spectrometry. So they're -- they're methods of analysis, and I have used them all.

Q. Are those methods of analysis expensive?

A. Very.

MS. METZINGER: Objection to the form.

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BY MS. MATUSCHAK:

Q. How expense effective would you say an HPLC analysis is?

A. You know, I really can't say because it depends on what you're analyzing. The machines are very expensive. So the machine that you need to accomplish the analysis could be a few hundred thousand dollars. Then when you're doing the analysis of particular substances, you have to get reagents and chemicals that could be quite expensive in addition to the machine. It's also fairly labor intensive, so you need staff who can spend time.

So I can't really give you an answer to how much it costs. It depends on the particular substance that you're analyzing.

Q. If the substance you were analyzing is apoaequorin, would that help you estimate what the cost would be to conduct such an analysis?

A. Personally, I could speak with colleagues and get advice from people about what it would cost if you -- if you wanted to know that information. There are some things that you need to have in order to do this kind of analysis. You

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have to have a standard. So you have to have a -- a known amount of this substance which you can use, and then they -- they could be quite expensive to develop. I've known people who have paid companies to create standards for them, and that is a very large upfront cost.

So that's something that I would have to look into. I wouldn't know that off the top of my head.

Q. Okay. Because I just -- sitting here today, you -- you don't have enough information to provide a cost estimate?

A. That's correct.

Q. And are you aware of anyone ever conducting an HPLC analysis on apoaequorin?

A. You know, I'm not. I'd have to look at the papers again to see if -- if the -- if the published papers analyzed apoaequorin. I don't recall right now.

Q. Okay. But just -- just sitting here today, you're not aware of such an analysis having been conducted?

A. Yes.

MS. METZINGER: Objection. Asked and answered.

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BY MS. MATUSCHAK:

Q. And your opinion is that the mechanism of action does not need to be known in order for a dietary supplement to be effective, correct?

A. Yes. In order for it to be effective and really in order -- yeah, in order for it to make a claim of effectiveness, a structure function claim.

Q. And so the mechanism action theories that you're advancing are possibilities but not proven mechanisms, correct?

A. That's correct.

MS. METZINGER: Objection to form.

THE WITNESS: And -- and there are -- there are lots of examples of substances that are used even as drugs for which we don't know the mechanism of action.

You know, aspirin was -- has been utilized since the late 1800s, and it's only in the 1970s or '80s that the mechanism of action was -- was used. I remember when I was in graduate school

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learning about this, the teacher used the word "miracle," that it was considered a miracle drug. It did all kinds of stuff but we didn't know why. But doctors still recommended it.

And corticosteroids, cortisone, is another one. Prednisone. For many years, that was prescribed without understanding the mechanism of action at all. Now we understand what the mechani- -- mechanism of action is of that.

So there are lots of examples even of drugs that are shown to be effective and are therefore utilized without knowing the mechanism of action.

BY MS. MATUSCHAK:

Q. Why did you think it was important to opine on the mechanism of action in this case?

MS. METZINGER: Objection.

And I would caution Dr. Kurzer that she not divulge any communications with counsel in providing an answer to

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this question. If she's able to answer the question without divulging such information, she's free to do so.

THE WITNESS: I would choose not to answer the question.

BY MS. MATUSCHAK:

Q. Do you think that the mechanism of action is relevant to an issue in this case?

MS. METZINGER: Objection.

THE WITNESS: I'm sorry. Can you repeat the question? I didn't catch one part of it.

BY MS. MATUSCHAK:

Q. Sure.

Do you think the mechanism of action is relevant to an issue in this case?

A. Is it relevant --

MS. METZINGER: Objection.

THE WITNESS: Is it relevant to the primary issue in this case?

BY MS. MATUSCHAK:

Q. To any issue in this case.

MR. de LEEUW: Object to the form. You're asking for a legal opinion?

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THE WITNESS: My --
BY MS. MATUSCHAK:
Q. Sorry.
A. My interpretation of the guidance, the FTC guidance, is that a mechan- -- a mechanism of action is not necessary, therefore it is not relevant.
MS. MATUSCHAK: Let's go off the record, please.
THE VIDEOGRAPHER: We are going off the record at 5:17 P.M.
(Off the record from 5:17 until 5:26.)
THE VIDEOGRAPHER: We're going back on the record at 5:26 P.M.
MS. MATUSCHAK: Thank you for your time, Dr. Kurzer. I don't have further questions at this time.
THE WITNESS: You're very welcome.
MS. METZINGER: I do not have any questions for Dr. Kurzer.
MR. de LEEUW: No questions. Thank you.
THE VIDEOGRAPHER: This

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concludes the video deposition Mindy Kurzer. We are going off the record at 5:26 P.M.
(Deposition concluded at 5:26 P.M.)

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STATE OF TENNESSEE)
COUNTY OF DAVIDSON) SS:
I, Gary Schneider, TLCR No. 676, in and for the State of Tennessee, do hereby certify:
That, prior to being examined, the witness named in the foregoing deposition was by me duly sworn to testify the truth, the whole truth and nothing but the truth;
That said deposition was taken down by me stenographically at the time and place therein named, and thereafter transcribed via computer-aided transcription under my direction, and the same is a true, correct and complete transcript of said proceedings;
Before completion of the deposition, review of the transcript was not requested. If requested, any changes made by the deponent (and provided to the reporter) during the period allowed are appended hereto.
I further certify that I am not interested in the outcome of the action.
Witness my hand this October 5, 2021.

s/Gary Schneider
GARY SCHNEIDER, TLCR No. 676
Certified Shorthand Reporter

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CERTIFICATE OF DEPONENT

I hereby certify that I have read and examined the foregoing transcript, and the same is a true and accurate record of the testimony given by me.

Any additions or corrections that I feel are necessary, I will attach on a separate sheet of paper to the original transcript.

I hereby certify, under penalty of perjury, that I have affixed my signature hereto on the date so indicated.

DATED:

_____
MINDY KURZER, Ph.D.

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WITNESS: MINDY KURZER, Ph.D.
DATE: SEPTEMBER 29, 2021
CASE: FTC, et al., v. QUINCY BIOSCIENCE HOLDING, ET AL.
Please note any errors and the corrections thereof on this errata sheet. The rules require a reason for any change or correction. It may be general, such as "To correct stenographic error," or "To clarify the record," or "To conform with the facts."

PAGE	LINE	CORRECTION	REASON FOR CHANGE

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UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK

FEDERAL TRADE COMMISSION and

THE PEOPLE OF THE STATE OF NEW YORK, by LETITIA JAMES, Attorney General of the State of New York,

Plaintiffs,

v.

QUINCY BIOSCIENCE HOLDING COMPANY, INC., a corporation;

QUINCY BIOSCIENCE, LLC, a limited liability company;

PREVAGEN, INC., a corporation d/b/a SUGAR RIVER SUPPLEMENTS;

QUINCY BIOSCIENCE MANUFACTURING, LLC, a limited liability company;

MARK UNDERWOOD, individually and as an officer of QUINCY BIOSCIENCE HOLDING COMPANY, INC., QUINCY BIOSCIENCE, LLC, and PREVAGEN, INC.; and

Defendants.

Case No. 1:17-cv-00124-LLS

ERRATA SHEET FOR THE TRANSCRIPT
OF THE DEPOSITION OF MINDY KURZER, Ph.D.

I, Mindy Kurzer, hereby make the following corrections to the transcript of my deposition, which occurred on September 29, 2021:

PAGE	LINE(S)	CORRECTION	REASON
14	16	Replace "1973" with "1974"	Incorrect
20	24	Replace "self-culture" with "cell-culture"	Transcription error
22	13	Replace "Loris Garby" with "Lars Garby"	Transcription error
34	19	Replace "and" with "of"	Transcription error
36	8	Replace "triable" with "tribal"	Transcription error
65	13	Replace "conscious" with "conscience"	Transcription error
102	19	Replace "canines" with "canine"	Transcription error
115	4	Replace "message" with "methods"	Transcription error
155	8	Replace "casing" with "casein"	Transcription error
180	6	Replace "ADL" with "LDL"	Transcription error
183	17	Replace "Jiam-Min" with "Jian-Min"	Transcription error
204	5	Replace "then" with "when"	Transcription error
246	4	Replace "enhanced" with "NHANES"	Transcription error
265	6	Replace "referred" to "refer"	Transcription error
266	3	Replace "RKTC" with "RCT"	Transcription error

283	8	Replace "?" with "."	Incorrect.

I declare under penalty of perjury under the laws of the United States of America that the foregoing is true and correct.

Executed on October 29, 2021.

MINDY KURZER